Thoughts?

Bruce

From: Lisa Graver

Sent: Wednesday, November 11, 2009 11:01 AM

To: Bruce Sullivan

Subject: FW: Oxycodone ER launch

Attorney-Client

Lisa Graver

Vice President-Intellectual Property



Actavis

200 Elmora Avenue # 908-659-2510 @ LGraver@actavis.com Elizabeth , NJ 07202 United States w www.actavis.com Internal VoIP number # 1202510

Please note that this e-mail and its attachments are intended for the named addressee only and may contain information that is confidential and privileged. If you have by coincidence or mistake or without specific authorization received this e-mail and its attachments we request that you notify us immediately that you have received them in error, uphold strict confidentiality and neither read, copy, nor otherwise make use of their content in any way Please note that the sender of this e-mail and its attachments is solely responsible for its content if it does not concern the operations of Actavis Group or its subsidiaries.

From: Michael Perfetto

Sent: Tuesday, November 10, 2009 12:50 PM

To: Lisa Graver; Doug Boothe

Cc: Jinping McCormick; Bob Miranda; Chris Gordon

Subject: FW: Oxycodone ER launch

Attorney-Client

PLAINTIFFS TRIAL EXHIBIT
P-01092_00001

Michael Perfetto VP, Sales and Marketing



Actavis

60 Columbia Rd. Bldg B #908-868-9778 @ mperfetto@actavis.com Morristown , NJ 07960 United States # 607-724-0322 w www.actavis.com Internal VoIP number

Please note that this e-mail and its attachments are intended for the named addressee only and may contain information that is confidential and privileged. If you have by coincidence or mistake or without specific authorization received this e-mail and its attachments we request that you notify us immediately that you have received them in error, uphoid strict confidentiality and neither read, copy, nor otherwise make use of their content in any way Please note that the sender of this e-mail and its attachments is solely responsible for its content if it does not concern the operations of Actavis Group or its subsidiaries.

From: Jinping McCormick

Sent: Tuesday, November 10, 2009 12:32 PM

To: Lisa Pehlke; Michael Berryman; Michael Dorsey; Michael Perfetto; Nancy Baran; Steve Cohen; Thad Demos;

Andrea Johnson; Bob Miranda; Chris Gordon; John Reed; Soojung Chung; Violet Wojtulewicz

Cc: David Myers; Karen Stoedter **Subject:** Oxycodone ER launch

All,

Enclosed please find the following information for Oxycodone ER launch:

- Sell sheet including PI can be sent to customers. Hard copies are being printed as we speak.
- · Product profile sheet
- Container labels
- PI
- HDMA forms

Please note the official name on the label is Oxycodone HCl **Controlled-release** Tablets. This tablets color and imprints are exactly the same as the brand.

Please take a look at the HDMA forms, pricing and let me know if anything needs to be corrected.

Jinping

HDMA Standard Product I	nformation
-------------------------	------------

Pharmaceutical Products

New Item	☐ Promotion/Deal	☐ Open Stock	☐ Post Launch Change
	Date:	Nov 24 2009	Page 1 of 2

PROD	UCT INFORMA	TION				SPEC	AL HANDLI	ING AND ST	ORAGE R	EQUIREM	IENTS	
Manufacturer/Broker Name: Actavis To	towa LLC N	umber: <u>52152</u>			a. Tempera	ture – Indi	cate the noi	mal tempera	ature range	for this p	roduct.	
Product Name: Oxycodone controlled r	elease tablets 8	0mg			I. Cont	rolled Ro	om Tempera	ture (68° – 7	7° F)	Σ	۵	
Product ID Number:							•	•	,	_		
NDC <u>52152-411-02</u>	⊠ UPC/G	STIN # <u>3 52152</u>	-411-02 0			-	ature (59° –	00° F)				
Description: Round, unscored, green-c	olored, convex	tablets imprint	ted with OC on	<u>one si</u> de	III. Exce	ssive Hea	t (>104° F)]	
and 80 on the other					IV. Cool	(46° – 59°	F)					
Address: 990 Riverview Drive					V. Refri	gerated (3	6° – 46° F)]	
City, State, Zip: Totowa, NJ 07512 Key Contact: Jinping McCormick		~~··			VI. Froz	en (-4° – 1	/ /0 E\				- 7	
Key Contact: Jinping McCormick Phone Number: 888-925-2342						-	•					
Phone Number:					VII. No R	equireme	nt				J	
Is the Product?					b. Are temp	erature ex	cursions pe	ermitted/allo	wed for pro	oduct?	∛ Yes	No
Is the Product a Controlled Drug? X	•	mp nem					-		-		3	
If Yes, Schedule Number: C II						•	•	iture range a	na nours a	iuration:		
Is this ARCOS reportable?							a		***************************************			
Is this Product a Legend Device?					c. Are there	additiona	ıl storage ar	nd shipping	requiremen	its?	Yes	⊠ No
Country of Origin: USA					If ves	. please p	rovide on p	age 2.				
Harmonization Code Number for Interna	tional Shipping	*			,	, p		-9				
Is this product a Hazardous Material or	Cytotoxic Agent	1?										
🗌 Yes 🛮 No If yes, p	rovide addition	al information	on page 2.									
Attach copy of Material Safety Data S	heet (MSDS)											
Attach Package Insert												
ADDITIONAL PRODUCT					ITEM AND PA	CKING IN	FORMATIO	N				
INFORMATION	Size/Strength	Unit	<u> </u>	Mst	r. Inner	Wght.		Case	lter	n	Pallet	# Cases/
Is there a minimum order quantity?	/Form	Of Sale	UPC Code			Lbs.	Cube	Dimensions	Dimens	sions D	imensions	
If yes, ☐ Case ☐ Carton ☒ Item		⊠ Bottle	Case:	48		Case:	0.37	Depth:	Depth:	De	epth:	
Number of Pieces? 48	100/80mg/	☐ Box				4.25 lb	cu ft	11.81"	1.83"	40)''	100
Shelf Life: 35 Months	CR Tablets	☐ Glass jar	Carton:			Carton:		Height:	Height:	He	eight:	
Whsl. Code #:		Ampule						7.38"	3.28"			
Fineline Code:		☐ Other	Item:			Item:		Width:	Width:	1	idth:	
Is Item? ☐ Unit Dose ☐ Unit of Use	For Generic D	l	3 5215241102		Aliana AD	1.34 oz		7.31"	1.63"	48	J.,	
If Unit Dose, is item bar coded to unit	Loi Geneiic r	nug mouducts			ting: <u>AB</u> iivalent: <u>OxyCo</u>				ct Color: gr		······	CD Toblet
dose for Hospital tracking purposes?			III. Dranu	ivame Equ		<u>/////////////////////////////////////</u>	TION	iv. Gener	ic Name FC	r brand. <u>C</u>	xycodone	CR Tablet
☐ Yes ☐ No			D 1 A11							. 5.0	000	
Will handling data change in the first:	Regu	lar	Purchase Allov		Distribution Al ☐ OI ☐		Invoice Cost (\$)	Net Cost (\$)	Mfr's AWP	Avg Retl Price (\$)		Excise Tax
6 months?	Cost		\$		\$	%	(*/		* .	1	(*)	
9 months? ☐ Yes	DZ			79								
12 months? 🔲 Yes	EA				<u> </u>		\$974.75		1170.17			
Unknown? ☐ Yes	PPK											
				_								

This offer is made on a proportionally equal basis to all sellers' accounts completive with customer.

Signature:

Copyright © 2005 by the Healthcare Distribution Management Association

Revised 02/21/06

Oxycodone CR Tablets Item Description: Manufacturer: Actavis Totowa LLC If additional information is necessary, provide on right of page or as attachment. HAZARDOUS MATERIAL INFORMATION ADDITIONAL INFORMATION AS NECESSARY Is this product: a) Cytotoxic? ☐ Yes ⊠ No ☐ Yes ⊠ No b) Carcinogen? c) Inhalation Hazard? ☐ Yes ⊠ No d) Contact Hazard? ☐ Yes ⊠ No Is this item considered a carcinogen? ☐ Yes ⊠ No ☐ Yes 🛛 No Is this item an aerosol requiring special storage? Does this product require special clean-up instructions? ☐ Yes 🛛 No If yes, attach MSDS with special instructions. Department of Transportation (DOT) I.D. Number: Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. □ ORGANIC ☐ ANTINEOPLASTIC ☐ INORGANIC ☐ STEROID/ANDROGEN ☐ CORROSIVE/OXIDIZER ☐ ESSENTIAL CHEMICAL ☐ AEROSOL ☐ PRECURSOR CHEMICAL (Describe below) ☐ AEROSOL CLASS ☐ MAXIMUM QTY LEVEL Is the product restricted for air shipping? Passenger ☐ Cargo ☐ Passenger & Cargo **Precursor Chemical:** Size/Strength **Ephedrine** ☐ Yes ⊠ No Pseudoephedrine ☐ Yes ⊠ No Phenylpropanolamine ☐ Yes ⋈ No ADDITIONAL STORAGE AND SHIPPING REQUIREMENTS Is this product to be shipped to customers on ice? ☐ Yes ⊠ No ☐ Yes ⊠ No Is this product to be shipped to customers on dry ice? Does this product require refrigerated truck for transport? ☐ Yes ☑ No Is this Product State Regulated? ☐ Yes ☐ No If yes, list states on the right or as an attachment. ☐ Yes Are there special returns requirements? ⊠ No If yes, provide requirements in the space to the right or as attachment.



Oxycodone Hydrochloride Controlled-Release Tablets CII



National Brand Name: OxyContin[®] Tablets

RX

OTC

Brand Manufacturer: Purdue Pharma L.P.

Therapeutic Rating: Compared to OxyContin[®] Tablets

Product Description: Active Ingredient: Oxycodone Hydrochloride

10 mg: Round, unscored, white-colored, convex tablets imprinted with OC on one

side and 10 on the other.

20 mg: Round, unscored, pink-colored, convex tablets imprinted with OC on one

side and 20 on the other.

40 mg: Round, unscored, yellow-colored, convex tablets imprinted with OC on

one side and 40 on the other.

80 mg: Round, unscored, green-colored, convex tablets imprinted with OC on one

side and 80 on the other.

Label: Actavis

Packaging Information:

	10 mg 100s	20 mg 100s	40 mg 100s	80 mg 100s
NDC Number:	52152-408-02	52152-409-02	52152-410-02	52152-411-02
UPC Number:	3 52152-408-02 0	3 52152-409-02 7 3 52152-410-02 3		3 52152-411-02 0
Case Quantity:	48 Bottles	48 Bottles 48 Bottles 48 Bottles		48 Bottles
Case Dimensions (LxWxH):	11.81" x 7.31" x 7.38" 11.81" x 7.31" x 7.38" 11.81" x 7.31" x 7.38"		11.81" x 7.31" x 7.38"	
Case Cube:	0.37 ft	0.37 ft	0.37 ft	0.37 ft
Case Weight:	4.25 lb	4.25 lb	4.25 lb	4.25 lb
Bottle Dimensions (HxDxW):	3.28" x 1.83" x 1.63"	3.28" x 1.83" x 1.63"	3.28" x 1.83" x 1.63"	3.28" x 1.83" x 1.63"
Bottle Weight:	1.34 oz	1.34 oz	1.34 oz	1.34 oz

^{*} OxyContin[®] is a registered trademark of Purdue Pharma L.P.

A253 Rev 10/2009

Each Controlled-Release
Tablet Contains:
Optional Contains:
Swall Own tablets whole. Do
not crush, Dreak, or chew.
Dispense in a light,
light-resistant container.
Store at 20"-25" (58"-77" F).
with excursions permitted
between 15"-30" (59"-86")
ISSE USP Contained Room
Temperature).
US. Patent Nos:

U.S. Patent Nos.: 5,508,042; 7,129,248



Each Controlled-Release
Tablet Contains:
Option Controlled Selease
Tablet Contains:
Option Controlled Selease
Some as 19th,
Ight-resistant container,
Store at 20"-25" (58"-37" F),
with excursions permitted
between 15"-30" (59"-86")
ISSE USP Controlled Room
Temperature).
US. Patent Nos:

U.S. Patent Nos.: 5,508,042; 7,129,248



Each Controlled-Release
Tablet Contains:
Optional Contains:
Swall Own tablets whole. Do
not crush, Dreak, or chew.
Dispense in a light,
light-resistant container.
Store at 20"-25" (58"-77" F).
with excursions permitted
between 15"-30" (59"-86")
ISSee USP Controlled Room
Temperature].
U.S. Patent Nos.

U.S. Patent Nos.: 5,508,042; 7,129,248



Each Controlled-Release
Tablet Contains:
Option Controlled Selease
Tablet Contains:
Option Controlled Selease
Option Controlled Selease
Selease
Selease
Swall Observe Selease
Sw

U.S. Patent Nos.; 5,508,042; 7,129,248



onwind. ycodone hydrochloride extended-release is an opioid ag-ist and a Schedule II controlled substance with an abuse

iability similar to morphine. Dxycodone can be abused in a manner similar to other opiol gonists, legal or illicit. This should be considered when pre scribing or dispensing oxycodone hydrochloride extended-re ease in situations where the physician or pharmacist i concerned about an increased risk of misuse, abuse, or diver

SION.

Oxycodone hydrochloride extended-release tablets are an extended-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

Oxycodone hydrochloride extended-release tablets are NOT

Oxycodone hydrochloride extended-release tablets are NOT intended for use as a prin analgesic.
Oxycodone hydrochloride extended-release 60 mg, 80 mg and 150 mg tablets, or a single dosse greater than 40 mg, ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. A single dosse greater than 40 mg or total daily dosse greater than 80 mg may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effect of opiods.
OXYCODONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS ARE TO BE SWALLOWED WHOLE AND ARE

80 mg for use in opiod-tolerant patients only 10 mg, 20 mg, 40 mg, 80 mg





NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OXYCODONE HO PROCHLORIDE EXTENDED FRELEASE TABLETS LEAD TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY EATAL DOSE OR OXYCODONE

Oxycodone hydrochloride extended-release tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths for oral administration. The tablet strengths describe the amount of oxycodone per tablet as the hydrochloride salt. The structural formula for oxycodone hydrochloride is as follows:

C_uH_nNO_vHCl MW 35.83

The chemical formula is 4,50-epoxy-14-hydroxy-3-methyoxy-17-methylmorphinan-6-one hydrochloride. Dxycodone is a white, oddrles crystallline powder derived from the opium alkaloid, thebaine. Oxycodone hydrochloride dissolves in water (1 g in 6 to 7 mL). It is slightly soluble in alcohol (octanol water arition coefficient 0.7). The tablets contain the following inactive ingredients: ammonio methacrylate copolymer, hypromellose, lactose, magnesium stearate, polyterhiene glycol 400, povidone, sodium hydroxide, sorbic acid, stearyl alcohol, talc, titanium dioxide, and triacetin.

The 10 mg tablets also contain: hydroxypropyl cellulose.

The 20 mg tablets also contain: polysorbate 80 and red iron oxide.

iron oxide. The 40 mg tablets also contain: polysorbate 80 and yellow

fron oxide. The 80 mg tablets also contain: FD&C blue No. 2, hydrox-

CLINICAL PHARMACOLOGY

Oxycodone is a pure agoinst opioid whose principal therapeutic action is analgesia. Other members of the class known as opioid agonists include substances such as morphine, hydromorphone, fentanyl, codeline, and hydrocodone. Pharmacological effects of opioid agonists include anxiolysis, euphoria, feelings of relaxation respiratory depression, constipation, miosis, and cough suppression, as well as analgesia. Like all pure opioid agoinst analgesis, with increasing doses there is increasing analgesia, unlike with mixed agonist/antagonists or non-

opioid analgesics, where there is a limit to the analgesic effect with increasing doses. With pure opioid agonist analgesics, there is no defined maximum dose, the ceiling to analgesic effectiveness is imposed only by side effects, the more serious of which may include somnolence and reprinted representation.

Central Nervous System The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and play a role in the

throughout the brain and spinal cord and play a role in the analgesic effects of this drug. Oxycodone produces respiratory depression by direct ac-tion on brain stem respiratory centers. The respiratory de-pression involves both a reduction in the responsiveness of the brain stem respiratory centers to increases in car-bon dioxide tension and to electrical stimulation. Oxyodone depresses the cough reflex by direct effect on the cough center in the medulla. Antifussive effects may occur with doses lower than those usually required for analgesia.

oia. done causes miosis, even in total darkness. Pinnoint pupils are a sign of oploid overdose but are not pathog-nomonic (e.g., portline lesions of hemorrhagic or ischemic origin may produce similar findings). Marked mydfasis rather than miosis may be seen with hypoxia in the setting of oxycodone hydrochloride extended-release overdose

of oxycodone hydrochloride extended-release overdose (See DVERDOSAG). Castrointestinal Tract And Other Smooth Muscle Oxycodone causes a reduction in molility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristattic waves in the colon are decreased, while tone may be increased to the point of spasm resulting in constipation. Other opioid-induced effects may include a reduction in gashire, biliary and parcreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase. Cardiovascular System
Oxycodone may produce release of histamine with or without associated peripheral vasodilation. Manifestations of histamine release and/or peripheral vasodilation may include purificiar, flushing, red eyes, sweating, and/or orthostatic hypotension.

clude pruritus, nusming, no static hypotension.

Concentration – Efficacy Relationships
Studies in normal volunteers and patients reveal predictable relationships between oxycodone dosage and plasma oxycodone concentrations, as well as between concentration and certain expected opioid reflects, such as pupillary constriction, sedation, overall "drug effect", analyesia and feelings of "relaxation".

tration for analgesia will vary widely among patients, espe tration for analgesia will vary widely among patients, espe-cially among patients who have been previously treated with potent agonist opioids. As a result, patients must be treated with individualized tritration of dosage to the desired effect. The minimum effective analgesic concentration of oxy-codone for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome and/or the development of an new pain concentration. Adverse Experience Relationships Doycodone hydrochloride extended-release tablets are as-ceptable with highest positions of the programment of

Oxycodone hydrochloride extended-release labilets are as sociated with typical opioid-related adverse experiences. There is a general relationship between increasing ox-codone plasma concentration and increasing frequency dose-related opioid adverse experiences such as nausa-vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation is altered by the deve

opment of tolerance to opioid-related slide effects, and the relationship is not clinically relevant. As with all opioids, the dose must be individualized (see DOSAGE AND ADMINISTRATION), because the effective analgesic dose for some patients will be too high to be tolerance.

analgesic dose for some patients will be too nigh to be tol-erated by other patients.

PHARMACOKINETICS AND METABOLISM

The activity of oxycodone hydrochloride extended-release tablets is primarily due to the parent drup oxycodone. Oxy-codone hydrochloride extended-release tablets are de-signed to provide controlled delivery of oxycodone over

22 hours. Breaking, chewing or crushing oxycodone hydrochloride extended-release tablets eliminates the controlled delivery mechanism and results in the rapid release and absorption

of a potentially fatal dose of oxycodone.

Oxycodone release from oxycodone hydrochloride extended-release tablets is pH independent. Oxycodone is well absorbed from oxycodone hydrochloride extended-release tablets with an oral bioavailability of 60% to 87%. The relative oral bioavailability of oxycodone hydrochl extended-release to immediate-release oral dosage forms is 100%. Upon repeated dosing in normal volunteers in pharmacokinetic studies, steady-state levels were achieved within 24-36 hours. Dose proportionality and/or bioavailability has been established for the 10 mg, 20 mg, bloavailability has been established for the 10 mg, 20 mg, 40 mg, 80 mg, and 160 mg tablet strengths for both peak plasma levels (C_{max}) and extent of absorption (AUC). Oxycodone is extensively metabolized and eliminated primarily in the urine as both conjugated and unconjugated metabolites. The apparent elimination half-life of oxycodone following the administration of oxycodone hydrochloride extended-release was 4.5 hours compared to 3.2 hours for immediate-release oxycodone.

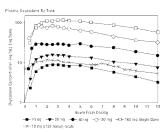
About 60% to 87% of an oral dose of oxycodone reache About 60% to 87% of an oral dose of oxycodone reaches the central compartment in comparison to a parenteral dose. This high oral bioavallability is due to low pre-systemic and/or first-pass metabolism. In normal volunters, the 1% of absorption is 0.4 hours for immediate-release oral oxycodone, in contrast, oxycodone hydrochlonide extended-release tablets exhibit a biphasic absorption pattern with two apparent absorption half-lives of 0.6 and 6.9 hours, which describes the initial release of oxycodone from the tablet followed by a prolonged release.

Plasma Oxycodone by Time
Dose proportionally has been established for the 10 mg.

Plasma Oxycodone by Time Dose proportionality has been established for the 10 mg. 20 mg, 40 mg, and 80 mg tablet strengths for both peak plasma concentrations ($C_{\rm max}/a$) and extent of absorption (ALIC) (see Table 1 below). Another study established that the 160 mg tablet is bioequivalent to 2 x 80 mg tablets as the 160 mg tablet is bioequivalent to 2 x 80 mg tablets as well as to 4 x 40 mg for both peak plasma concentrations (C_{max}) and extent of absorption (AUC) (see Table 2 below). Given the short half-life of elimination of oxy-codone from oxycodone hydrochloride extended-release stady-state plasma concentrations of oxycodone are achieved within 24-36 hours of initiation of dosing with

oxycodone hydrochloride extended-release tablets. In a study comparing 10 mg of oxycodone hydrochloride ex-tended-release every 12 hours to 5 mg of immediate-re-lease oxycodone every 6 hours, the two treatments were found to be equivalent for AUC and C_{max}, and similar for

Cmin (trough) concentrations



Regimen/ Dosage Form	AUC (ng+hr/mL)†	C _{max} (ng/mL)	T _{max} (hrs)	Trough Canc. (ng/mL)
Single Dose 10 mg Oxycodone Hydrochlonde Extended-release	100.7 [26.6]	10.6 [20.1]	2.7 [44.1]	n.a.
20 mg Oxycodone Hydrochloride Extended-release	207.5 [35.9]	21.4 [36.6]	3.2 [57.9]	n.a.
40 mg Oxycodone Hydrochloride Extended-release	423.1 [33.3]	39.3 [34.0]	3.1 [77.4]	n.a.
80 mg Oxycodone Hydrochloride Extended-release*	1085.5 [32.3]	98.5 [32.1]	2.1 [52.3]	n.a.
Multiple Dose 10 mg Oxycodone Tablets q12h	103.6 [38.6]	15.1 [31.0]	3.2 [69.5]	7.2 48.
5 mg immediate- release q6h	99.0 [36.2]	15.5 [28.8]	1.6 [49.7]	7.4 [50.

Regimen/ Dosage Form	AUC == (ng+hr/mL) ¹	C _{max} (ng/mL)	T _{max} (hrs)	Trou Cor (ng/i
Single Dose 4 x 40 mg Oxycodone Hydrochloride Extended-release*	1935.3 [34.7]	152.0 [28.9]	2.56 [42.3]	n
2 x 80 mg Oxycodone Hydrochloride Extended-release*	1859.3 [30.1]	153.4 [25.1]	2.78 [69.3]	n
1 x 160 mg Oxycodone Hydrochloride Extended-release*	1856.4 [30.5]	156.4 [24.8]	2.54 [36.4]	n

Oxycodone hydrochloride Extended-Release is NOT INDI-CATED FOR RECTAL ADMINISTRATION. Data from a study involving 21 normal volunteers show that oxycodone hy-drochloride extended-release tablets administered per recdrochloride extended-release tablets administered per rec-tum resulted in an AUC 59% greater and a C_{max} 9% higher than tablets administered by mouth. Therefore, there is an increased risk of adverse events with rectal administration. Food Effects Food has no significant effect on the extent of absorption of oxycodone from oxycodone hydrochloride extended-re-

lease. However, the peak plasma concentration of oxy-codone increased by 25% when a oxycodone hydrochloride extended-release 160 mg tablet was admin-istered with a high-fat meal. Distribution

Distribution
Following intravenous administration, the volume of distribution (Vss) for oxycodone was 2.6 L/kg. Oxycodone binding to plasma protein at 37°C and a ph of 7.4 was about 45%. Once absorbed, oxycodone is distributed to keletal muscle, liver, intestinal tract, lungs, spleen, and brain. Oxycodone has been found in breast milk (see PRE-

CAUTIONS): Metabolism oxycodone hydrochloride is extensively metabolized to noroxycodone, oxymorphone, and their glucuronides. The major circulating metabolite is noroxycodone with an AUC ratio of 0.6 relative to that of oxycodone. Noxycodone is reported to be a considerably weaker analgesic than oxycodone. Oxymorphone, although oxpessing analgesic activity, is present in the plasma only in low concentrations. The correlation between oxymorphone concentrations and opioid effects was much less than that seen with exycodone plasma concentrations. The analgesic activity.

oxycodone plasma concentrations. The analgesic activity profile of other metabolites is not known. The formation of oxymorphone, but not noroxycodone, is mediated by cytochrome P450 2D6 and, cytochrome P450. 344, respectively. In addition, noroxymorphone formation is mediated by both cytochrome P450 2D6 and cytochrome P450 3A4. Therefore, the formation of these metabolites can in theory be affected by other drugs (see Drug-Drug Interactions).

Dxycodone and its metabolites are excreted prim the kidney. The amounts measured in the urine have been reported as follows: free oxycodone up to 19%; conjugated oxycodone up to 50%; free oxymorphone 0%; conjugated oxymorphone $\leq 14\%$, both free and conjugated noroxycodone have been found in the urine but not quantified. The total plasma clearance was 0.8 L/min for adults Special Populations

affected by age, being 15% greater in elderly as compared

to young subjects. **Gender** Fernale subjects have, on average, plasma oxycodone con-centrations up to 25% higher than males on a body weight adjusted basis. The reason for this difference is unknown.

Renal Impairment
Data from a pharmacokinetic study involving 13 patients
with mild to severe renal dysfunction (creatinine clearance
<60 ml/min) show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, codone concentrations SU% and 20% higher, respectively, and AUC values for oxycodone, noroxycodone, and oxymorphone 60%, 50%, and 40% higher than normal subjects, respectively. This is accompanied by an increase in sedation but not by differences in respiratory rate, pupillary constriction, or several other measures of drug effect. There was an increase in the of elimination for oxycodone of only 1 hour (see PRECAUTIONS). Hepatic Impairment

Data from a study involving 24 patients with mild to moderate hepatic independing show pack plasma oxycodone and provi-

Data from a study involving 24 patients with millio to mouerate hepatic dysfunction show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, than normal subjects. ALIC values are 95% and 65% higher, respectively. Oxymorphone peak plasma concentrations and AUC values are lower by 30% and 40%.

These differences are accompanied by increases in some, but

not other, drug effects. The t1/2 elimination for oxycodone in

Oxycodone is metabolized in part by cytochrome P45 2D6 and cytochrome P450 3A4 and in theory can be at fected by other drugs. Oxycodone is metabolized in part by cytochrome P450 206 to oxymorphone which represents less than 15% of the total administered dose. This route of elimination may be blocked by a variety of drugs (e.g., certain cardiovas-cular drugs including amiodarone and quindine as well as polycyclic anti-depressants). However, in a study involving

> A single-dose, double-blind, placebo- and dose-controlled A single-dose, double-blind, placebo- and dose-controlled study was conducted using oxycdone hydrochloride extended-release (10, 20, and 30 mg) in an analgesic pain model involving 182 patients with moderate to severe pain. Twenty and 30 mg of oxycodone hydrochloride extended-release were superior in reducing pain compared with placebo, and this difference was statistically significant. The onset of analgesic action with oxycodone hydrochloride extended-release occurred within 1 hour in most patients following oral administration.
>
> CLINICAL TRIALS.
>
> A double-blind relacebo-controlled fixed-dose parallel.

CLINICAL TRIALS

A double-blind placebo-controlled, fixed-dose, parallel group, two-week study was conducted in 133 patients with chronic moderate to severe pain, who were judged as having inadequate pain control with their current therapy. In this study, 20 mg oxycodone hydrochloride extended-release q12h but not 10 mg oxycodone hydrochloride extended-release q12h docreased pain compared with placebo, and this difference was statistically soinfificant.

INDICATIONS AND USAGE

INDICATIONS AND USAGE
Oxycodone hydrochloride extended-release tablets are an extended-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. Oxycodone hydrochloride extended-release is NOT in-

Oxycodone hydrochloride extended-release is NOT inended for use as a prin analgesic.
Physicians should individualize treatment in every carinitiating therapy at the appropriate point along a progression from non-opioid analgesics, such as nonsteroidal anti-Inflammatory drugs and acetaminophen
to opioids in a plan of pain management such as outlined by the World Health Organization, the Agency for
Healthcare Research and Quality (formerly known as the
Agency for Health Care Policy and Research), the Foderation of State Medical Boards Model Guidelines, or the
merison Pain Society.

eration of State Medical Boards Model Guidelines, or the American Pain Society.

Oxycodone hydrochloride extended-release is not indi-cated for pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild or not expected to persist for an extended period of time Oxycodone hydrochloride extended-release is only indi-cated for postoperative use the patients at leady receiv-ing the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians Should individualize

extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

CONTRAINDICATIONS

CONTRAINDICATIONS

Obycodome hybrot chloride extended-release is contraindicated in patients with known hypersensivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hyperarchia. Oxycodone hydrochloride extended-release is contraindicated in any patient who has or is suspected of having parafetic lieus.

is contraindicated in any patient who has or is suspected of having paralytic ileus.

WARNINGS

OXYCODONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED OXYCODONE HYDROCHLORIDE EXTENDED RELEASE TABLETS LEADS TO RAPID RELEASE TABLETS LEADS TO RAPID RELEASE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF DXYCODOME.

DXYCOGONE MYDROCHORIDE STRENDED RELEASE TABLETS LEADS OF THE PARALY PATALY PATAL DOSE OF DXYCODOME.

Oxycodone hydrochloride extended-release 60 mg, 30 mg and 160 mg tablets or a single dose greater than 40 mg, ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. Misuse, Abuse and Diversion of Opioids

Oxycodone is an opioid agonist of the morphine-type. Such drugs are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Oxycodone can be abused in a manner similar to other op-oid agonists, legal or illicit. This should be considered when prescribing or dispensing oxycodone hydrochloride ex tended-release in situations where the physician or phar macist is concerned about an increased risk of misuse abuse, or diversion.

ne hydrochloride extended-release has been re oxycoobne hydrochlorode extended-release has been re-ported as being abused by crushing, chewing, snorting, or injecting the dissolved product. These practices will re-sult in the uncontrolled delivery of the oploid and pose a significant risk to the abuser that could result in overdose and death (see WARNINGS and DRUG ABUSE AND AD-DICTION).

DICTION).

Concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

Healthcare professionals should contact their State Professional Licensing Board, or State Controlled Substances Authority for information on how to prevent and delect pather professional Licension of the profession.

abuse or diversion of this product.

Interactions with Alcohol and Drugs of Abuse
Oxycodone may be expected to have additive effects when
used in conjunction with alcohol, other optoids, or illicit

drugs that cause central nervous system depression.

ORUG ABUSE AND ADDICTION

DRUG ABUSE AND ADDICTION
Oxycodone hydrochloride extended-release is a mu-agonist opioid with an abuse liability similar to morphine and
is a Schedule II controlled substance. Oxycodone, like morphine and other opioids used in analgesia, can be

abused and is subject to criminal diversion.

Drug addiction is characterized by compulsive use, use for normalical purposes, and continued use despite harm or risk of harm. There is a potential for drug addiction to develop following exposure to opioids, including oxycodone.

Drug addiction is a treatable disease, utilizing a multi-disci

Drug addiction is a treatable disease, utilizing a mutil-disci-plinary approach, but relapse is common.

"Drug-seeking," behavior is very common in addicts and drug abusers. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo ap-propriate examination, testing or referral, repeated "loss" of prescriptions, tempering with prescriptions and reluctance to provide prior medical records or contact information for other treating physician(s). "Doctor shopping" to obtain ad-ditional prescriptions is common among drug abusers and people suffering from untreated addiction.

Abuse and dictions are senared and distinct from physical

people suffering from untreated addiction.
Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addiction and is characterized by misuse for non-medical purposes, often in combination with other psychoactive substances. Oxycodone hydrochloride extended-release, like other opioids, has been diverted for non-medical use. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests is strongly advised.

rised.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Oxycodone hydrochloride extended-release consists of a dual-polymer matrix, intended for oral use only. Abuse of the crushed tablet poses a hazard of overdose and death. This risk is increased with concurrent abuse of alcohol and other substances. With parenteral abuse, the tablet excellent and other substances. ents, especially talc, can be expected to result in local tis see necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with trans-mission of infectious diseases such as hepatitis and HIV.

Respiratory Depression
Respiratory Depression is the chief hazard from oxycodone, the active ingredient in oxycodone hydrochloride extended-release, as with all opioid agonists. Respiratory depression is a particular problem in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that

depress respiration.
Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease of oxyconone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve. hypoxia, hypercapina, or presiding respiratory depression, in such patients, even usual therapeutic doses of oxycordone may decrease respiratory drive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed and to the patients. be employed only under careful medical supervision at the

Head Injury
The respiratory depressant effects of opioids include carbon The respiratory depressant effects of opioids include carbon dioxide retention and secondary elevation of cuebrospinal fluid pressure, and may be markedly exaggerated in the presence of head injury, intracarallal tesions, or other sources pre-existing increased intracrantal pressure. Oxycadone produces effects on pupillary response and consciousness which may obscure neurologic signs of further increases in intracranial pressure in patients with head injuries.

Hypotensive Effect Oxycodinen hydrochloride extended-release may cause se-vere hypotension. There is an added risk to individuals whose ability to maintain blood pressure has been comprised by a depleted blood volume, or after concurrent ad-ministration with drugs such as phenothiazines or other agents which compromise vasomotor tone. Oxycodone may produce orthostatic hypotension in ambulatory pa-tients. Oxycodone, like all opioid analgesics of the mor-phine-type, should be administered with caution to patients in circulatory shock since vasontiation morphicated in the

Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined with ONS depressant drugs, and should be reserved for cases where the benefits of opioid analgesia outweigh the known risks of respiratory depression, altered mental state, and postural hypotension.

Use of oxycodone hydrochloride extended-release is asso-Use of oxycodome hydrocinonice extended-release is asso-cated with increased potential risks and should be used only with caution in the following conditions: acute alco-holism; adrenocortical insufficiency (e.g., Addison's dis-ease). CNS depression or coma, delirium tremens, debigated patients, lyphosocolicois associated with respe-ratory depression; myxedema or hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of he-patic, pulmonary or renal function; and toxic psychosis. The administration of oxycodone may obscure the diagno-sis or clinical curuse in natients with acute abdiomizal consis or clinical course in patients with acute abdominal co ditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

gravate seizures in some clinical settings. Interactions with other CNS Depressants Interactions with other CNS Depressants
Oxycodone hydrochloride extended-release should be used
with caution and started in a reduced dosage (1/3 to 1/2 of
the usual dosage) in patients who are concurrently receiving
other central nervous system depressants including sectatives
or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol. Interactive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result if these drugs are taken in combination with the usual doses of oxycodone hydrochloride extended-release. Interactions with Mixed Agonist/Antagonist Opioid Anal-

gesics Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, and butorphanol) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as oxycodone. In this situation, mixed agonist/analagonist analgesics may reduce the analgesic effect of oxycodone and/or may precipi-

duce the analyseis effect of oxycodone and/or may precipitate withdrawal symptoms in these patients.

Ambulatory Surgery and Postoperative Use
Oxycodone hydrochloride extended-release is not indicated for pre-emptive analyseis (administration pre-operatively for the management of postoperative pain).
Oxycodone hydrochloride extended-release is not indicated for pain in the immediate postoperative period (the first 12 to 24 hours following surgery) for patients not pre-iously taking the drug, because its safety in this setting has not been established.

Oxycodone hydrochloride extended-release is not indi-

has not been established.
Oxycodone hydrochloride extended-release is not indi-cated for pain in the postoperative period if the pain is mild or not expected to persist for an extended period of time.
Oxycodone hydrochloride extended-release is only indi-

PATIENT INFORMATION **OXYCODONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS** 10 mg, 20 mg, 40 mg, 80 mg*

*80 mg for use in opiod-tolerant patients only.



R Only Read this information carefully before you take oxycodone hydrochloride extended-release tablets.

Also read the information you get with your refills. There may be something new. This information does not take the place of talking with your doctor about your medical condition or your treatment. Only you and your doctor can decide if oxycodone hydrochloride extended-release is right for you. Share the important information in this leaflet with members of your household.

What Is The Most Important Information I Should Know About Oxycodone Hydrochloride Extended-Release?

- Use oxycodone hydrochloride extended-release the way your doctor tells you to.
- Use oxycodone hydrochloride extended-release only for the condi-
- tion for which it was prescribed. Oxycodone hydrochloride extended-release is not for occasional ("as needed") use.
- Swallow the tablets whole. Do not break, crush, dissolve, or chew them before swallowing. Oxycodone hydrochloride extended-release works properly over 12 hours only when swallowed whole. If a tablet is broken, crushed, dissolved, or chewed, the entire 12 hour dose will be absorbed into your body all at once. This can be dangerous, causing an overdose, and possibly death.
- Keep oxycodone hydrochloride extended-release out of the reach of **children**. Accidental overdose by a child is dangerous and may result in death.
- Prevent theft and misuse. Oxycodone hydrochloride extended-release contains a narcotic painkiller that can be a target for people who abuse prescription medicines. Therefore, keep your tablets in a secure place, to protect them from theft. Never give them to anyone else. Selling or giving away this medicine is dangerous and against the law.

What is Oxycodone Hydrochloride Extended-Release?

Oxycodone hydrochloride extended-release is a tablet that comes in several strengths and contains the medicine oxycodone (ox-e-KOEdone). This medicine is a painkiller like morphine. Oxycodone hydrochloride extended-release treats moderate to severe pain that is expected to last for an extended period of time. Use oxycodone hydrochloride extended-release regularly during treatment. It contains enough medicine to last for up to twelve hours.

Who Should Not Take Oxycodone Hydrochloride Extended-Release? Do not take oxycodone hydrochloride extended-release if

- your doctor did not prescribe oxycodone hydrochloride extended-release for you.
- your pain is mild or will go away in a few days.
- your pain can be controlled by occasional use of other painkillers.
- you have severe asthma or severe lung problems. you have had a severe allergic reaction to codeine, hydrocodone, dihy-
- drocodeine, or oxycodone (such as Tylox, Tylenol with Codeine, or Vicodin). A severe allergic reaction includes a severe rash, hives, breathing problems, or dizziness.
- you had surgery less than 12 24 hours ago and you were not taking oxycodone hydrochloride extended-release just before surgery.

Your doctor should know about all your medical conditions before deciding if oxycodone hydrochloride extended-release is right for you and what dose is best. Tell your doctor about all of your medical problems, especially the ones listed below:

- trouble breathing or lung problems
- head injury
- liver or kidney problems adrenal gland problems, such as Addison's disease
- convulsions or seizures
- alcoholism
- hallucinations or other severe mental problems past or present substance abuse or drug addiction
- If any of these conditions apply to you, and you haven't told your doctor, then you should tell your doctor before taking oxycodone hydrochloride

extended-release. If you are pregnant or plan to become pregnant, talk with your doctor. Oxycodone hydrochloride extended-release may not be right for you.

Tell your doctor if you are breast feeding. Oxycodone hydrochloride

extended-release will pass through the milk and may harm the baby. Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. They may cause serious medical problems when taken with oxycodone hydrochloride extended-release, especially if they cause drowsiness.

How Should I Take Oxycodone Hydrochloride Extended-Release?

- Follow your doctor's directions exactly. Your doctor may change your dose based on your reactions to the medicine. Do not change your dose unless your doctor tells you to change it. Do not take oxycodone hydrochloride extended-release more often than prescribed.
- Swallow the tablets whole. Do not break, crush, dissolve, or chew before swallowing. If the tablets are not whole, your body will absorb too much medicine at one time. This can lead to serious problems, including overdose and death.
- If you miss a dose, take it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not take 2 doses at once unless your doctor tells you to.
- In case of overdose, call your local emergency number or Poison Control Center right away.
- Review your pain regularly with your doctor to determine if you still need oxycodone hydrochloride extended-release.
- You may see tablets in your stools (bowel movements). Do not be concerned. Your body has already absorbed the medicine.

If you continue to have pain or bothersome side effects, call your doc-

Stopping oxycodone hydrochloride extended-release. Consult your doctor for instructions on how to stop this medicine slowly to avoid uncomfortable symptoms. You should not stop taking oxycodone hydrochloride extended-release all at once if you have been taking it for more than a few

After you stop taking oxycodone hydrochloride extended-release, flush the unused tablets down the toilet.

What Should I Avoid While Taking Oxycodone Hydrochloride Extended-Release?

- Do not drive, operate heavy machinery, or participate in any other possibly dangerous activities until you know how you react to this medicine. Oxycodone hydrochloride extended-release can make you sleepy.
- Do not drink alcohol while using oxycodone hydrochloride extendedrelease. It may increase the chance of getting dangerous side effects. • Do not take other medicines without your doctor's approval. Other
- medicines include prescription and non-prescription medicines, vitamins, and supplements. Be especially careful about products that make you

What are the Possible Side Effects of Oxycodone Hydrochloride Extended-Release?

Call your doctor or get medical help right away if

vour breathing slows down

• you feel faint, dizzy, confused, or have any other unusual symptoms Some of the common side effects of oxycodone hydrochloride extendedrelease are nausea, vomiting, dizziness, drowsiness, constipation, itching, dry mouth, sweating, weakness, and headache. Some of these side effects may decrease with continued use.

There is a risk of abuse or addiction with narcotic painkillers. If you have abused drugs in the past, you may have a higher chance of developing abuse or addiction again while using oxycodone hydrochloride extended-

These are not all the possible side effects of oxycodone hydrochloride extended-release. For a complete list, ask your doctor or pharmacist.

General Advice About Oxycodone Hydrochloride Extended-Release Do not use oxycodone hydrochloride extended-release for conditions for which it was not prescribed.

 Do not give oxycodone hydrochloride extended-release to other people, even if they have the same symptoms you have. Sharing is illegal and may cause severe medical problems, including death.

This leaflet summarizes the most important information about oxycodone hydrochloride extended-release. If you would like more information, talk with your doctor. Also, you can ask your pharmacist or doctor for information about oxycodone hydrochloride extended-release that is written for health professionals.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Distributed by: Actavis Totowa LLC, 990 Riverview Drive, Totowa, NJ 07512 USA 8949-00 Rev. 05/09 cated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize appropriate (See American Pain Society guidelines).
Patients who are already receiving axycodone bydrochl

Patients who are already receiving oxycodone hydrochloride extended-release tablets as part of ongoing analgesic therapy may be safely continued on the drug if appropriate dosage adjustments are made considering the procedure, other drugs given, and the temporary changes in physiology caused by the surgical intervention (see DOSAGE AND AD-MINISTRATION).

rochloride extended-release and other mor-Oxycodone hydrochloride extended-release and other mor phine-like opioids have been shown to decrease bowe phine-like oploids have been shown to decrease bowel motility, lete is a common postoperative complication, especially after intra-abdominal surgery with opioid analgesia. Caution should be taken to monitor for decreased bowel motility in postoperative patients receiving oploids. Standard supportive therapy should be implemented.

Wes in Pancreatic@illiary Tract Disease

Dxycodone may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatilis. Opioids like oxycodone may cause increases in the servina manylase level.

ease, including acute pancrealitis. Opioids like oxycodone may cause increases in the serum amylase level.

Tolerance and Physical Dependence
Tolerance is the need for increasing doses of oploids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.
The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness. lacrimation, rhinorrhea, yawning, perspiration, chills, myaglia, and mydriasis. Other symptoms also may develop, including; including

uon, minurines, yawining, perspirationi, ronis, myaqias, romiydrasis, Other symptoms also may develop, including; ii-ritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anoreva, vomitting, diarrhea, or increased blood pressure, respiratory rate, or heart rate, in general, poliosis should not be abruptly discontinued (see DOSAGE AND ADMINISTRATION: Cessation of Therapy). Information, for Patient (Pragado).

Information for Patients/Caregivers
If clinically advisable, patients receiving oxycodone hydrochloride extended-release tablets or their caregivers should be given the following information by the physician

- tended-release tablets contain oxycodone, which is a mor-phine-like substance

 2. Patents should be advised that oxycodone hydrochloride extended-release tablets were designed to work properly only if swallowed whole. Oxycodone hydrochloride ex-tended-release tablets will release all their contents at once if broken, chewed, or crushed, resulting in a risk of fatal overfose. Patients should be advised to report episodes of break-

- overdose.

 2. Patients should be advised to report episodes of break-through pain and adverse experiences occurring during therapy, Individualization of dasage is essential to make optimal use of this medication.

 Patients should be advised not to adjust the dose of oxy-codone hydrochloride extended-release without consulting the prescribing professional.

 Patients should be advised that oxycodone hydrochloride extended-release may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating heavy machinery).

 Patients should not combine oxycodone hydrochloride extended-release with alcohol or other central nervous system depressants (sleep aids, tranquilizars) except by the orders of the prescribing physicals because dangerous additive effects any occur resulting in serious injury or death.

 Women of childbearing potential who become, or are planning to become, pregnant should be advised to consult their physician reparting the effects of analgesiscs and other drug.

 Patients should be advised that oxycodone hydrochloride extended-release is a potential drug of abuse. They should proted if thom theft, and it should never be given to aryone that the midden and the should be advised that they may be should proted if thom theft, and it should never be given to aryone the should be advised that they may pass se might matrix.
- Patients should be advised that they may pass empty matrix "ghosts" (tablets) via colostomy or in the stool, and that this is of no concern since the active medication has already been 10. Patients should be advised that if they have been receiving
- eathers should be advessed told in high great peed in Sectional for treatment with oxycordone hydrochloride extended-release for more than a few weeks and cessation of herapy is indicated. It may be appropriate to taper the oxycordone hydrochloride by the propriate to taper the oxycordone hydrochloride high propriate hydrochloride hyd

Use in Drug and Alcohol Addiction

use in urug and Alcohol Addiction
Oxycodone hydrochloride extended-release is an opioid with
no approved use in the management of addictive disorders.
Its opportunge in individuals with drug or alcohol dependence, either active or in remission, is for the management
of pain requiring opioid analgesia.

Prug-Drun Interactions

or pain requiring opinion analysisa.

Drug-Drug Interactions

Opioid analgesics, including oxycodone hydrochloride extended-release, may enhance the neuromuscular blocking action of skeletal muscle releasants and produce an increased degree of respiratory depression. uegree or respiratory depression.
Oxycodone is metabolized in part by cytochrome P450 2D6
and cytochrome P450 3A4 and in theory can be affected by

and cytocritoric Preso Service (1) and to the drugs of the drugs (1) condone is metabolized in part to oxymorphone via cytochrome P450 2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs including amiodarone and quinidine as well as polycyclic artidepressants), such blockade has not yet been shown to be of clinical significance with this agent. Clinicians should be aware of this possible interaction, however.

Use with CNS Depressants Use with CNS Depressants Oxycodone hydrochloride extended-release, like all opioid analgesics, should be started at 1/3 to 1/2 of the usual dosage in patients who are concurrently receiving other cen-tral nervous system depressants including sedatives or hypnous, general anesthetics, phenothiszines, centrally acting anti-emetics, tranquilizers and alcohol because respiratory depression, hypotension, and profound sedation or coma may result. No specific interaction between oxycodone and monoamine oxidase inhibitors has been observed, but caution in the use of any opioid in patients taking this class of drugs is sporrough.

drugs is appropriate. Carcinogenesis, Mutagenesis, Impairment of Fertility Studies of oxycodone to evaluate its carcinogenic potential have not been conducted.

Oxycodone was not mutagenic in the following assays:

Ames Salmonella and E. coil test with and without metabolic activation at doses of up to 5000 mcg, chromosomal aberation test in human lymphocytes in the absence of metabolic activation at doses of up to 1500 mcg/mL, and with activation 48 hours after exposure at doses of up to 5000 mcg/mL and in the in vive bone marrow micronucleus test in mice (at plasma levels of up to 48 mcg/mL). Oxycodone was clastogenic in the human lymphocyte chromosomal assay in the presence of metabolic activation in the human chromosomal aberration test (at greater than or equal to 1250 mcg/mL), at 24 but not 48 hours of exposure and in the mouse lymphoma assay at doses of 50 mcg/mL or greater with metabolic activation and at 400 µg/mL or greater with metabolic activation and at 400 µg/mL or reater with metabolic activation and at 400 µg/mL or ater without metabolic activation.

Pregnancy
Terdappent Effects - Category B: Reproduction studies have been performed in rats and rabbits by oral administration at doses up to 8 mg/kg and 125 mg/kg, respectively. These doses are 3 and 46 times a human dose of 160 mg/day, based on mg/kg basis. The results did not reveal evidence of harm to the fetus due to oxygodone. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always orediched.

no adequate and well-controlled studies in pregnant women. Because animal peroduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Oxycodone hydrochloride extended-release is not recommended for use in women during and immediately prior to labor and delivery because oral opioids may cause respiratory depression in the newborn. Reportate whose mothers have been taking oxycotone chronically may exhibit respirator depression; and for withdraul semborne, author vital response or the response of the response o ratory depression and/or withdrawal symptoms, either at

birth and/or in the nursery.

Nursing Mothers

Low concentrations of oxycodone have been detected in Low concentrations of oxycodone have been detected in breast milk Whitdrawl symptoms can occur in breast-leed-ing infants when maternal administration of an opioid anal-gesic is stopped. Ordinarily, mursing should not be undertaken while a patient is receiving oxycodone by-drochloride extended-release because of the possibility of sedation and/or respiratory depression in the infant.

ended-release have not been established in pediatric pa-ents below the age of 18. It must be remembered that xycodone hydrochloride extended-release tablets cannot e crushed or divided for administration.

be crushed or divided for administration. Geriatric Use In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone appeared to be slightly reduced. Compared to young adults, the plasma concentrations of oxycodone were increased approximately 15% (see PHARMACOKINETICS AND METABOLISM). Of the total number of subjects (445) in clinical studies of oxycodone hydrochloride extended-release, 148 123 and have an 65 and halfer (including those age 75 and halfer). studies of oxycodone hydrochlonde extended-release, 148 (33.3%) were age 65 and older (including those age 75 and older) while 40 (9.0%) were age 75 and older. In clinical trials with appropriate initiation of therapy and dose titration, no untoward or unexpected side effects were seen in the elderly patients who received oxycodone hydrochloride exeny patients with exerved oxycutorie hydrochiorne ex-tended-release. Thus, the usual doses and dosing intervals are appropriate for these patients. As with all opticids, the starting dose should be reduced to 1/3 to 1/2 of the usual dosage in debilitated, non-tolerant patients. Respiratory deussage in usumated, non-tolerant patients. Respiratory de-pression is the chief hazard in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

centrations of the active drug substance may be of value in

selected, unusual or complex cases. Hepatic Impairment A study of oxycodone hydrochloride extended-release in p A study of oxycodone hydrochloride extended-release in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 1/3 to 1/2 the usual doses and careful dose litration is warranted.

In patients with renal impairment, as evidenced by decreased creatinine clearance (-60 mL/min), the concentrations of oxycodone in the plasma are approximately 50% higher than in subjects with normal renal function. Dose initiation should

in subjects with normal renal function. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

Gender Differences

In pharmacokinetic studies, oploid-nalive females demonstrate up to 25% higher average plasma concentrations and greater frequency of typical oploid adverse events than males, even after adjustment for body weight. The clinical relevance of a difference of this magnitude is low for a drug intended for chronic usage at individualized dosages, and there was no male/female difference detected for efficacy or adverse events in clinical trials.

there was no male/female difference detected for efficacy or adverse events in clinical trials. **ADVERSE REACTIONS**The safety of oxycodone hydrochloride extended-release was evaluated in double-blind clinical trials involving 713 patients with moderate to severe pain of various stillogies, in open-label studies of cancer pain, 187 patients received oxycodone hydrochloride extended-release in total daily doses rangling from 20 mg to 640 mg per day. The average total daily dose was approximately 105 mg per day. Serious adverse reactions which may be associated with oxycodone hydrochloride extended-release tablet therapy in clinical use are those observed with other opid analgesics. including respiratory depression, apnea, respiratory arrest, and (to an even lesser degree) circulatory depression, hydrogression, hydrogre

including respiratory depression, apnea, respiratory arrest, and (to an even lesser depre-p circulatory depression, hypotension, or shock (see OVERDOSAGE). The non-serious adverse events seen on initiation of therapy with oxycodone hydrochloride extended-release are typical opicid side effects. These events are dose-dependent, and their frequency depends upon the dose, the clinical setting, the patient's level of opicid tolerance, and host factors specific to the individual. They should be expected and managed as a nort of opicid snalepsis. The most fereure (1.59%), in the control of the control of the control opicid snalepsis. The most fereure (1.59%) in the control opicid snalepsis. The most fereure (1.59%) in the control opicid snalepsis. cific to the individual. They should be exected and manage as a part of opioid analgesia. The most frequent (5%) in-clude: constipation, nausea somnolence, dizziness, vernit-ing, prurflus, headache, dry mouth, sweating, and asthenia in many cases the frequency of these events during initiation of therapy may be minimized by careful individualization of starting dosage, slow literation, and the avoidance of large swings in the plasma concentrations of the opioid. Many of these adverse events will cease or decrease in intensity as poxycodone hydrochloride extended-release therapy is coninued and some degree of tolerance is developed

The following adverse experiences were reported in exvcodone hydrochloride extended-release-treated patients with an inci-dence between 1% and 5%. In descending order of frequency they were anorexia, nervousness, insormia, tever, confusion, diarrhea, abdominal pain, dyspepsia, rash, anxiety, euphoria, dyspnea, postural hypotension, chills, twitching, gastritis, abormal dreams, thought abnormalities, and hiccups

normal dreams, thought abnormalibes, and niccups. The following adverse reactions occurred in less than 1% of patients involved in clinical trials or were reported in post-marketing experience.

Blood and lymphalic system disorders: lymphadenopathy

drawal)

Ear and labyrinth disorders: tinnitus

Endocrine disorders: syndrome of inappropriate antidiuretic
hormone secretion (SIADH)

normone secretion (SIADIH) Eye disorders: abnormal vision Gastrointestinal disorders: dysphagia, eructation, flatulence, gastrointestinal disorder, ileus, increased appetite, stomattiis General disorders and administration site conditions: chest pain, edema, facial edema, malaise, pain, periphera edema, thirst, withdrawal syndrome (with and withou seizures)
Immune system disorders: anaphylactic or anaphylactoid

reaction (symptoms of)
Infections and infestations: pharyngitis
Injury, poisoning and procedural complications: accidental in

Investigations: hyponatremia, increased hepatic enzymes,

Metabolism and nutrition disorders: dehydration
Musculoskeletal and connective tissue disorders: neck pani **Nervous system disorders:** abnormal gait, amnesia, hyper:

netrous sysuem usoruers: aonomial gait, amnesia, hyper-kinesia, hyperionia (muscular), hypesthesia, hypotonia, mi-graine, paresthesia, seizures, speech disorder, stupor, syncope, taste perversion, tremor, vertigo Psychiatric disorders: agitation, depresonalization, depres-sion, emotional lability, hallucination Renal and urinary disorders: dysuria, hematuria, polyuria, urinary reterition, urination immaired

urinary referition, urination impaired Reproductive system and breast disorders: amenorrhea, decreased libido, impotence Respiratory, thoracic and mediastinal disorders: cough in-creased, volice alteration Skin and subcutaneous tissue disorders: dry skin, exfolia-tive dermatilis, uriticaria

Vascular disorders: vasodilation
OVERDOSAGE

OVERDOSAGE

Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flacidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death.

Constricted pupils, bradycardia, hypotension, and death because and constructions of the construction of the

of case reports has indicated that the risk of fatal overdose is further increased when oxycodone hydrochloride ex-bended-release is abused concurrently with alcohol or other. CNS depressents, including other opioids. In the Irealment of oxycodone overdosage, primary attention should be given to the re-establishment of a patent arising and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

or defibrillation.

The pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. In patients who are physically denednent on any opioid agonist including oxycodone hydrochloride extended-release, an abrupt or compilete reversal of opioid effects may precipitate an acute abstinence syndrome. The severity of the withdrawal syndrome produced will depend on the degree of physical dependence and the dose of the antagonist administrations. physical dependence and the dose of the antagonist adr istered. Please see the prescribing information for the cific opioid antagonist for details of their proper use. DOSAGE AND ADMINISTRATION

General Principles
OXYCODONE HYDROCHLORIDE EXTENDED-RELEASE IS AN OPIOID AGONIST AND A SCHEDULE II CONTROLLED SUBSTANCE WITH AN ABUSE LIABILITY SIMILAR TO MORPHINE. OXYCODONE. LIKE MORPHINE AND OTHER OPIOIDS USED IN ANALGESIA. CAN BE ABUSED AND IS SUBJECT AS COMMINAL DIPROCION.

SUBJECT TO CRIMINAL DIVERSION.
0XYCODONE HYDROCHLORIDE EXTENDED-RELEASE
TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT
TO BE BROKEN, CHEWED, OR CRUSHED, TAKING BROKEN, CHEWED, OR CRUSHED, TAKING BROKEN, CHEWED, OR CRUSHED DAYCODONE HYDROCHLO-KEN, CHEWED, OR CRUSHED DXYCODONE HYDROCHLO-RIDE EXTENDED-RELEASE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

One oxycodone hydrochloride extended-release 160 mg tablet is comparable to two 80 mg tablets when taken on an empty stomach. With a high-lat meal, however, there

is a 25% greater peak plasma concentration following one 160 mg tablet. Dietary caution should be taken when pa-tients are initially titrated to 160 mg tablets (see DOSAGE AND ADMINISTRATION).

Patients should be started on the lowest appropriate dose (see DOSAGE AND ADMINSTRATION: Initiation of Therapy). In treating DOSAGE AND ADMINISTRATION: Initiation of Therapy). In reating plan it is vital to assess the patient regularly and systematically. Therapy should also be regularly reviewed and adjusted based upon the patient's own reports of pain and side effects and the health professional is clinical judgment. Oxycodone hydrochloride extended-release tablets are an extended-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analogsic is needed for an extended period of time. The extended-release nature of the formulation allows oxycodone hydrochloride extended-release to be effectively administered every 12 hours (see CLINICAL PHARIMACOLOGY, PHARIMACOKNETICS AND METABOLISM). While symmetric (same dose AM and PM), around-the-clock, q12h dosing is appropriate

for the majority of patients, some patients may benefit from asymmetric (different dose given in AM than in PM) dosing, tallored to their pain pattern. It is usually appropriate to treat a patient with only one opioid for around-

gressive plan of pain management such as outlined by the World Health Organization, the American Pain Society and the Federation of State Medical Boards Model Guidelines. Healthcare professionals should follow appropriate pain management principles of careful assessment and oning monitoring (see BOXED WARNING). Initiation of Therapy It is critical to initiate the dosing regimen for each patient in-

dividually, taking into account the patient's prior opioid and orvolusity, taking time account the patients is prior option in non-optioid analysis is treatment. Attention should be given to: (1) the general condition and medical status of the patient. (2) the daily dose, potency, and kind of the analysis (s) the patient has been taking; (3) the reliability of the conversion estimate used to calculate the dose of cocycodone; (4) the patient's optioid exposure and opioid tolerance (if any);

(4) the patient's opioid exposure and opioid tolerance (if any); (5) the Special Instructions for exycodone hydrochloride ex-lended-release 60 mg, 80 mg and 160 mg Tablets or a single dose greater than 40 mg, and (6) the balance between pain control and adverse experiences. Care should be taken to use low initial doses of oxycodone hydrochloride extended-release in patients who are not al-ready opioid-tolerant, especially those who are receiving concurrent treatment with muscle releasants, sedatives, or other CNS colories. Perceivings. There is a perceiving concurrent treatment with muscle releasants, sedatives, or the CNS colories.

other CNS active medications (see PRECAUTIONS: Drug Orug Interactions).

Experience indicates a reasonable starting dose of oxycodone hydrochloride extended-release for patients who

codone hydrochloride extended-release for patients wino are taking non-opioid analgesics and require continuous around-the-clock therapy for an extended period of time is 10 mg q12h. If a non-opioid analgesic is being provided, it may be continued. Oxycodone hydrochloride extended-release should be individually titrated to a dose that provides adequate analgesis and minimizes side effects. For initiation of oxycodone hydrochloride extended-release heart for patients provinged hydrochloride extended-release therapy for patients provinged hydrochloride extended-release. For initiation of oxycoronic injuriscentificial extendior-tensas threapy for patients previously klading opiolist, the conversion ratios from Foley, KM. [NEJM, 1985; 313:84-95]. found below, are a reasonable starting point, although not verified in well-controlled, multiple-dose trials. I. Using standard conversion ratio estimates (see Table 4 below), multiply the my/day of the previous opioids by the appropriate multiplication factors to obtain the equivalent total daily dose of oral oxycordone.

of oxycodone hydrochloride extended-release.

3. Round down to a dose which is appropriate for the tablet strengths available.

4. Discontinue all other around-the-clock opioid drugs when oxycodone hydrochloride extended-release therapy is initiated.

5. No fixed conversion ratio is likely to be satisfactory in all partients, especially patients receiving large opioid doses. The recommended doses shown in Table 4 are only a starting priest and close observation and foreural triction are interest.

((Mg/Day Prior Opioid x Factor = Mg/Day Oral Oxycodone)							
	Oral Prior Opioid	Parenteral Prior Opioid						
Exycodone	1	**						
Codeine	0.15							
fydrocodone	0.9							
fydromorphone	4	20						
Evorphanol	7.5	15						
Aeperidine	0.1	0.4						
Aethadone	1.5	3						
Aorphine	0.5	3						
To be used only to	conversion to oral exyco	done. For patients receiving high-dose						
arenteral opioids, a m	ore conservative conversion	is warranted. For example, for high-dose						
	o 1.5 instead of 3 as a mult							

In all cases, supplemental analgesia should be made available in the form of a suitable short-acting analgesic. Oxycodone hydrochloride extended-release can be safely used concomitantly with usual doses of non-opioid analgesics and analgesic adjuvants, provided care is taken to select a proper initial dose (see PRECAUTIONS). Conversion from Transdermal Fentanyl to Oxycodone Hydrochloride Extended-Release
Eighteen hours following the removal of the transdermal fentanyl natch, oxycodone hydrochloride axtended-release

tanyl patch, oxycodone hydrochloride extended-release treatment can be initiated. Although there has been no systematic assessment of such conversion, a conservative cycle codone dose, approximately 10 mg q12h of oxycodon hydrochloride extended-release, should be initially substi

hydrochloride extended-release, should be initially substi-tuted for each 25 mcg/hr lentany transdermal path. The patient should be followed closely for early titration, as there is very limited clinical experience with this conversion.

Managing Expected Opioid Adverse Experiences
Most patients receiving opioids, especially those who appoid-naive, will experience side effects. Frequently the side effects from oxycodone hydrochloride extended-release are transient, but may require evaluation and management. Ad-verse events such as constipation should be anticipated and treated aggressively and prophylacitically with a stimulant laxative and/or stool softener. Patients do not usually be-come folerant to the constipation effects of opioids.

come tolerant to the constipating effects of opioids.

Other opioid-related side effects such as sedation and nausea are usually self-limited and often do not persist beyond
the first few days. If nausea persists and is unacceptable to
the patient, treatment with antiemetics or other modalities

the first few days. If nausea persists and is unacceptable to the patient, treatment with antiemetics or other modalities may relieve these symptoms and should be considered. Patients receiving oxycodone hydrochloride extended-release may pass an intact matrix "ghost" in the stool or via colostomy. These ghosts contain little or no residual oxycodone and are of no clinical consequence. Individualization of Dosage Once therapy is initiated, pain relief and other opioid effects should be frequently assessed. Patients should be thread to adequate effect (generally mild or no pain with the regular use of no more than two doses of supplemental analyseis per 24 hours.) Patients who experience breakthrough pain may require dosage adjustment or rescue medication. Because steady-state plasma concentrations are approximated within 24 to 36 hours, dosage adjustment may be carried out every 1 to 2 days. It is most appropriate to increase the q12h dose, not the dosing frequency. There is no clinical information on dosing intervals shorter than q12h. As a guideline, the total daily oxycodone dose usually can be increased by 25% to 55% of the current dose at each increase. It signs of excessive opioid-related adverse experiences are observed. He next dose may be reduced if this adjustment leads to inadequate analgesia, a supplemental dose of immediate-release exocordone may be deven. leads to inadequate analgesia, a supplemental dose of imme-diata-release oxycodone may be given. Alternatively, non-opi-oid analgesic adjuvants may be employed. Dose adjustments should be made to obtain an appropriate balance between pain relief and opioid-related adverse experiences. If significant adverse events occur before the therapeutic goal of mild or no pain is achieved, the events should be

nr control. no periods of changing analgesic requirements, includ-

the main training and the caregiver/dramity. Special Instructions for Oxycodone Hydrochloride Extended-Release Tablets 60 mg, 80 mg, and 160 mg or a single dose greater than 40 mg (for use in opioid-tolerant nations).

angle uous greater than 40 mg (tor use in uppliot-toerain patients only). Dxycodome hydrochloride extended-release 60 mg, 80 mg, and 160 mg lablets, or a single dose greater than 40 mg, are for use in opioid-tolerant patients only. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

One oxycodome hydrochloride extended-release 160 mg tablet is comparable to two 80 mg tablets when taken on

an empty stomach. With a high-fat meal, however, there is a 25% greater peak plasma concentration following nor 160 mg tablet. Dietary coution should be taken wher patients are initially titrated to 160 mg tablets.

Supplemental Analgesia
Most patients given around-the-clock therapy with cor
troiled-release opioids may need to have immediate-re
lease medication available for exacerbations of pain or t vent pain that occurs predictably during certain patien

prevent pain that occurs predictably during certain patient activities (ncident pain)

Maintenance of Therapy
The intent of the titration period is to establish a patient-specific q17d dose that will maintain adequate analgesia with acceptable side effects for as long as pain relief is necessary. Should pain recur then the dose can be incrementally increased to re-establish pain control. The method of therapy adjustment outlined above should be employed to re-establish pain control. During chronic therapy, specially for non-cancer pain syndromes, the continued need for around-the-clock opioid therapy should be reassessed periodically (e.g., every 6 to 12 months) as appropriate.
Cessation of Therapy
When the patient no longer requires therapy with oxy-codone hydrochloride extended-release tablets, doses should be tapered gradually to prevent signs and symptoms of withdrawal in the physically dependent patient.

Conversion from Oxycodone Hydrochloride Extended-Re lease to Parenteral Opioids

ose, conservative dose conversion ratios SAFETY AND HANDLING

SAFETY AND HANDLING
Oxycodone hydrochloride extended-release tablets are solid desage forms that contain oxycodone which is a controlled substance. Like morphine, oxycodone is controlled under Schedule II of the Controlled Substances Act.
Oxycodone hydrochloride extended-release has been targeted for thet and diversion by criminals. Healthcare professionals should contact their State Professional Licensing Board or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.
HOW SUPPLIED
Oxycodone Hydrochloride Extended-Release Tablets are

HOW SUPPLIED
Oxysodone Hydrochloride Extended-Release Tablets are
available as follows:
Oxydodone hydrochloride extended-release tablets 10 mg
are round, unscored, white-colored, convex tablets imare round, unscored, white-colored, convex tablets im-printed with OC on one side and 10 on the other. They are supplied as follows. Child resistant closure, opaque plastic bottes of 100 (MDC 54152-469-02). Oxycotone hydrochloride extended-release tablets 20 mg are round, unscored, pink-colored, convex tablets imprinted with OC on one side and 20 on the other. They are supplied

with Co of the state and 20 of the other. They are supplied as follows: Child resistant closure, opaque plastic bottles of 100 (NDC 52152-409-02).

Oxycodone hydrochloride extended-release tablets 40 mg

ted with OC on one side and 40 on the other. They are supplied as follows: Child resistant closure, opaque plastic bottles of 100 (NDC 52152-410-02). Oxycodone hydrochloride extended-release tablets 80 mg are round, unscored, green-colored, convex tablets im-printed with OC on one side and 80 on the other. They are

printed with OC on one side and ocon in equal, supplied as follows: Child resistant closure, opaque plastic bottles of 100 (NDC 52152-411-02).

Store at 20°-25°C (68°-77°F); with excursions permitted between 15°-30°C (59°-86°F)[See USP Controlled Room Temperature). ise in å tight, light-resistant container.

CAUTION DEA Order Form Required. **C**actavis

Distributed by: Actavis Totowa LLC 990 Riverview Drive Totowa, NJ 07512 USA 8949-00

HDMA Standard Product I	nformation
-------------------------	------------

Pharmaceutical Products

New Item	☐ Promotion/Deal ☐ Open Stock	☐ Post Launch Chang
	Date: Nov 24, 2009	Page 1 of 2

												J
PROD	UCT INFORMA	TION				SPEC	AL HANDLI	ING AND ST	ORAGE R	EQUIREM	ENTS	
Manufacturer/Broker Name: Actavis To	towa LLC N	umber: <u>52152</u>			a. Temperat	ture – Indi	cate the nor	mal tempera	ature range	for this pr	oduct.	
Product Name: Oxycodone controlled r	elease tablets 1	0mg			I. Controlled Room Temperature (68° – 77° F)						1	
Product ID Number:					. , ,						_	
NDC 52152-408-02	🛛 UPC/0	STIN # <u>3 52152</u>	-408-02 0			-	•	00-17			_	
Description: Round, unscored, white-co	olored, convex t	ablets imprint	ed with OC on or	ne side			t (>104° F)					
Address: 990 Riverview Drive					IV. Cool	(46° – 59°	F)				j	
City, State, Zip: Totowa, NJ 07512					V. Refri	gerated (3	6° – 46° F)]	
Key Contact: Jinping McCormick	F:	ax:			VI. Froze	en (-4° – 1	4° F)]	
Phone Number: 888-925-2342					VII. No R	eguireme	nt				1	
Phone Number:					7111 110 11					h		
Is the Product?	Drop S	hip Item			b. Are temp	erature ex	cursions pe	ermitted/allo	wed for pro	oduct? 🗵	Yes	☐ No
Is the Product a Controlled Drug? 🛛 Y	′es 🗌 No				If Yes	s, provide	the tempera	ture range a	nd hours o	duration:		
If Yes, Schedule Number: CII						-	·	-				
Is this ARCOS reportable?	′es □ No				_			900000000000000000000000000000000000000				
Is this Product a Legend Device?	′es ⊠ No				c. Are there	additiona	ıl storage ar	nd shipping	requiremer	nts?] Yes	⊠ No
Country of Origin: USA		***************************************			If yes	, please p	rovide on pa	age 2.				
Harmonization Code Number for Interna												
Is this product a Hazardous Material or	-											
☐ Yes 🛭 No If yes, p		al information	on page 2.									
Attach copy of Material Safety Data Si	heet (MSDS)											
Attach Package Insert	<u> </u>											
ADDITIONAL PRODUCT INFORMATION				30"	TEM AND PA	CKING IN	FORMATIO	N				
Is there a minimum order quantity?	Size/Strength /Form	Unit Of Sale	UPC Code	Mstr Shpr		Wght. Lbs.	Cube	Case Dimensions	Iter Dimen		Pallet mensions	# Cases/ Pallet
If yes, ☐ Case ☐ Carton ☒ Item	7111.1	⊠ Bottle	Case:	48	. Gust i k	Case:	0.37	Depth:	Depth:		pth:	1 4.100
Number of Pieces? 48	100/10mg/	☐ Box				4.25 lb	cu ft	11.81"	1.83"	40	•	100
Shelf Life: 35 Months	CR Tablets	 ☐ Glass jar	Carton:			Carton:		Height:	Height:	Не	ight:	
Whsl. Code #:		☐ Ampule						7.38"	3.28"			
Fineline Code:		☐ Other	Item:			Item:		Width:	Width:		dth:	
Is Item? Unit Dose Unit of Use			3 5215240802 0			1.34 oz		7.31"	1.63"	48		
	For Generic D	rug Products	9		-				ct Color: W			
If Unit Dose, is item bar coded to unit dose for Hospital tracking purposes?			III. Brand N	ame Equi	valent: OxyCo		man at 1.1	IV. Gener	ic Name Fo	or Brand: <u>C</u>	xycodone	CR Tablet
Yes No		1				INFORM/	TION			1	1	
			Purchase Allow		istribution All		Invoice	Net	Mfr's	Avg Reti	SRP	Excise
Will handling data change in the first: 6 months? ☐ Yes	Regu Cost	(4)	OI B	- 1	OI		Cost (\$)	Cost (\$)	AWP	Price (\$)	(\$)	Tax
9 months?	DZ	(<i>Ψ)</i>	\$	% \$		%		+			+	
12 months? Yes	EA						\$152.67		\$183.28			
Unknown? Yes	PPK						,	1	,			
										•	•	

This offer is made on a proportionally equal basis to all sellers' accounts completive with customer.

Signature:

Copyright © 2005 by the Healthcare Distribution Management Association

Revised 02/21/06

Oxycodone CR Tablets Item Description: Manufacturer: Actavis Totowa LLC If additional information is necessary, provide on right of page or as attachment. HAZARDOUS MATERIAL INFORMATION ADDITIONAL INFORMATION AS NECESSARY Is this product: a) Cytotoxic? ☐ Yes ⊠ No ☐ Yes ⊠ No b) Carcinogen? c) Inhalation Hazard? ☐ Yes ⊠ No d) Contact Hazard? ☐ Yes ⊠ No Is this item considered a carcinogen? ☐ Yes ⊠ No ☐ Yes 🛛 No Is this item an aerosol requiring special storage? Does this product require special clean-up instructions? ☐ Yes 🛛 No If yes, attach MSDS with special instructions. Department of Transportation (DOT) I.D. Number: Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. □ ORGANIC ☐ ANTINEOPLASTIC ☐ INORGANIC ☐ STEROID/ANDROGEN ☐ CORROSIVE/OXIDIZER ☐ ESSENTIAL CHEMICAL ☐ AEROSOL ☐ PRECURSOR CHEMICAL (Describe below) ☐ AEROSOL CLASS ☐ MAXIMUM QTY LEVEL Is the product restricted for air shipping? Passenger ☐ Cargo ☐ Passenger & Cargo **Precursor Chemical:** Size/Strength **Ephedrine** ☐ Yes ⊠ No Pseudoephedrine ☐ Yes ⊠ No Phenylpropanolamine ☐ Yes ⋈ No ADDITIONAL STORAGE AND SHIPPING REQUIREMENTS Is this product to be shipped to customers on ice? ☐ Yes ⊠ No ☐ Yes ⊠ No Is this product to be shipped to customers on dry ice? Does this product require refrigerated truck for transport? ☐ Yes ☑ No Is this Product State Regulated? ☐ Yes ☐ No If yes, list states on the right or as an attachment. ☐ Yes Are there special returns requirements? ⊠ No If yes, provide requirements in the space to the right or as attachment.

HDMA Standard Product I	nformation
-------------------------	------------

Pharmaceutical Products

New Item	☐ Promotion/Deal	☐ Open Stock	☐ Post Launch Chang
	Date: 1	Nov 24 2009	Page 1 of 3

												J
PROD	UCT INFORMA	TION				SPECI	AL HANDLI	ING AND ST	ORAGE R	EQUIREN	MENTS	
Manufacturer/Broker Name: Actavis To	towa LLC N	umber: <u>52152</u>			a. Temperat	ure – Indi	cate the noi	rmal tempera	ature range	for this p	roduct.	
Product Name: Oxycodone controlled r	elease tablets 2	0mg			I. Contr	olled Roo	om Tempera	iture (68° – 7	7° F)	Ē	⊠	
Product ID Number:							-	•	,	_		
NDC 52152-409-02	🛛 UPC/G	STIN # <u>3 52152</u>	-409-02 7			•	ature (59° –	00° F)				
Description: Round, unscored, pink-co and 20 on the other	lored, convex ta	blets imprinte	d with OC on one	side	III. Exces	ssive Hea	t (>104° F)			[
Address: 990 Riverview Drive					IV. Cool	(46° – 59°	F)			[
City, State, Zip: Totowa, NJ 07512					V. Refri	gerated (3	6° – 46° F)			[
Key Contact: Jinping McCormick	E				VI. Froze	n (-4° – 1				Г		
Phone Number: 888-925-2342						•	•			_		
Phone Number:					VII. No Re	equireme	TIL.			L		
Is the Product?					b. Are tempe	erature ex	cursions pe	ermitted/allo	wed for pro	oduct?	⊠ Yes [☐ No
Is the Product a Controlled Drug?		-			If Yes	provide	the tempera	iture range a	and hours o	luration:		
If Yes, Schedule Number: C II						9 -86F	-	and				
Is this ARCOS reportable?	′es □ No							***************************************	***************************************			
Is this Product a Legend Device?	∕es ⊠ No				c. Are there	additiona	ıl storage ar	nd shipping	requiremen	its? [] Yes [⊠ No
Country of Origin: USA					If yes,	please p	rovide on pa	age 2.				
Harmonization Code Number for Interna	ational Shipping						_					
Is this product a Hazardous Material or	Cytotoxic Agent	1?										
🗌 Yes 🛮 No If yes, p		al information	on page 2.									
Attach copy of Material Safety Data S	heet (MSDS)											
Attach Package Insert	T											
ADDITIONAL PRODUCT INFORMATION				IT	EM AND PAG	CKING IN	FORMATIO	N				
Is there a minimum order quantity?	Size/Strength	Unit		Mstr.	Inner	Wght.		Case	Iter		Pallet	# Cases/
If yes, ☐ Case ☐ Carton ☒ Item	/Form	Of Sale	UPC Code	Shpr.	Case Pk	Lbs.	Cube	Dimensions			imensions	Pallet
Number of Pieces? 48	400/20===/	⊠ Bottle	Case:	48		Case:	0.37	Depth:	Depth:		epth: 0"	400
	100/20mg/ CR Tablets	Box	Carton:	_	-	4.25 lb	cu ft	11.81"	1.83"		-	100
Shelf Life: 35 Months	CR Tablets	☐ Glass jar ☐ Ampule	Carton.			Carton:		Height: 7.38"	Height: 3.28"	"	eight:	
Whsl. Code #:		☐ Other	Item:			Item:		Width:	Width:	V	/idth:	
Fineline Code:			3 5215240902 7			1.34 oz		7.31"	1.63"		8"	
Is Item? Unit Dose Unit of Use	For Generic D	rug Products	<u> </u>	look Ratin	na: AB	1.0-1-02			ct Color: P	<u>_</u>	-	
If Unit Dose, is item bar coded to unit			III. Brand Na		-	ntinr			_		Oxycodone	CR Tablet
dose for Hospital tracking purposes?					COSTI	NFORMA	TION					
☐ Yes ☐ No			Purchase Allowa	nce Di	stribution All	owance	Invoice	Net	Mfr's	Avg Ret	SRP	Excise
Will handling data change in the first:	Regu	lar	OI BB		□ OI □		Cost (\$)	Cost (\$)	AWP	Price (\$	1 1	Tax
6 months?	Cost	(\$)	\$	% \$		%						
9 months? Yes	DZ					-	¢202.42		#2E0 00			
12 months?	EA PPK						\$292.12		\$350.69			
Unknown? Tes	IFN									1		

This offer is made on a proportionally equal basis to all sellers' accounts completive with customer.

Signature:

Copyright © 2005 by the Healthcare Distribution Management Association

Revised 02/21/06

Oxycodone CR Tablets Item Description: Manufacturer: Actavis Totowa LLC If additional information is necessary, provide on right of page or as attachment. HAZARDOUS MATERIAL INFORMATION ADDITIONAL INFORMATION AS NECESSARY Is this product: a) Cytotoxic? ☐ Yes ⊠ No ☐ Yes ⊠ No b) Carcinogen? c) Inhalation Hazard? ☐ Yes ⊠ No d) Contact Hazard? ☐ Yes ⊠ No Is this item considered a carcinogen? ☐ Yes ⊠ No ☐ Yes 🛛 No Is this item an aerosol requiring special storage? Does this product require special clean-up instructions? ☐ Yes 🛛 No If yes, attach MSDS with special instructions. Department of Transportation (DOT) I.D. Number: Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. □ ORGANIC ☐ ANTINEOPLASTIC ☐ INORGANIC ☐ STEROID/ANDROGEN ☐ CORROSIVE/OXIDIZER ☐ ESSENTIAL CHEMICAL ☐ AEROSOL ☐ PRECURSOR CHEMICAL (Describe below) ☐ AEROSOL CLASS ☐ MAXIMUM QTY LEVEL Is the product restricted for air shipping? Passenger ☐ Cargo ☐ Passenger & Cargo **Precursor Chemical:** Size/Strength **Ephedrine** ☐ Yes ⊠ No Pseudoephedrine ☐ Yes ⊠ No Phenylpropanolamine ☐ Yes ⋈ No ADDITIONAL STORAGE AND SHIPPING REQUIREMENTS Is this product to be shipped to customers on ice? ☐ Yes ⊠ No ☐ Yes ⊠ No Is this product to be shipped to customers on dry ice? Does this product require refrigerated truck for transport? ☐ Yes ☑ No Is this Product State Regulated? ☐ Yes ☐ No If yes, list states on the right or as an attachment. ☐ Yes Are there special returns requirements? ⊠ No If yes, provide requirements in the space to the right or as attachment.

HDMA Standard Product I	nformation
-------------------------	------------

Pharmaceutical Products

New Item	☐ Promotion/Deal ☐ Open Stock	☐ Post Launch Chang
	Date: Nov 24, 2009	Page 1 of 2

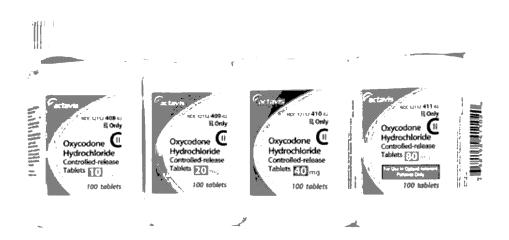
Manufacture/Broken Name: Additional Stockas LLC Number 82152													3
Product IN Name: Dxycoding controlled release tablets 40mg Product IN Name P	PROD	UCT INFORMA	TION				SPEC	IAL HANDL	ING AND ST	ORAGE R	EQUIRE	MENTS	
Product D Number:	Manufacturer/Broker Name: Actavis To	towa LLC N	umber: <u>52152</u>			a. Tempera	ture – Ind	icate the noi	rmal tempera	ature range	for this p	roduct.	
Product D Number	Product Name: Oxycodone controlled r	elease tablets 4	0mg			I. Cont	rolled Ro	om Tempera	ature (68° – 7	7° F)		abla	
Security					***************************************			-	•	,			
No. Cool (46° - 59° F)	NDC 52152-410-02	🛛 UPC/0	STIN # <u>3 52152</u>	2-410-02 3			•	•	00° F)				
Address: 980.Riverview.Drive.	· · · · · · · · · · · · · · · · · · ·	colored, convex	tablets imprii	nted with OC on	one_	III. Exce	ssive Hea	at (>104° F)			l		
V. Refrigerated (36° - 46° F)						IV. Cool	(46° – 59	° F)			[
Fax						V. Refri	gerated (36° – 46° F)			[
None Number:		E-				VI Froz	en (_4º 1	4∘ F \			ſ	7	
Phone Number							•	•					
St the Product St t						VII. NOR	equireme	nt			L		
Step Product a Controlled Drug? Yes No 1f Yes, Schedule Number: CI 59-86F 3nd 159-86F 3nd 15						b. Are temp	erature e	xcursions pe	ermitted/allo	wed for pro	oduct? [⊠ Yes	□No
If Yes, Schedule Number: C	•	•				-		-		-			
Set his ARCOS reportable?						į .	•	•	_	ina noars c	adiation.		
If yes, please provide on page 2.	Is this ARCOS reportable?	′es 🗌 No				-			***************************************				
Harmonization Code Number for International Shipping:	Is this Product a Legend Device?	∕es ⊠ No				c. Are there	addition	al storage ar	nd shipping i	requiremer	nts? [Yes	⊠ No
Statis product a Hazardous Material or Cytotoxis Agent? Yes No If yes, provide additional information on page 2.	Country of Origin: USA					If yes	, please p	rovide on p	age 2.				
Attach copy of Material Safety Data Sheet (MSDS) Attach Package Insert: ADDITIONAL PRODUCT INFORMATION Is there a minimum order quantity? If yes, Case Carto Stem Modern Stem Modern Mod	Harmonization Code Number for Interna	ational Shipping	:										
Attach copy of Material Safety Data Sheet (MSDS)	-	-											
Attach Package Insert			al information	on page 2.									
ADDITIONAL PRODUCT INFORMATION Is there a minimum order quantity? If yes,		heet (MSDS)											
Is there a minimum order quantity? If yes, Case Carton Item Number of Pieces? 48 100/40mg/ Box Carton: Item: Number of Pieces? 48 100/40mg/ Box Carton: Item: Ampule Stellator Stellat		I											
If yes, Case Carton Steme a minimum order quantity? If yes, Case Carton Steme Allowance Carton: Car					*	TEM AND PA	CKING IN	IFORMATIC	N				
If yes, Case Carton Sitem Number of Pieces? 48 100/40mg/ Box Case: 48 Case: 0.37 Carton: Carton: Height: 1.83" 40" 100	Is there a minimum order quantity?			LIDO Cada				Cuba					
Number of Pieces? 48	, ,	/FOIII				r. Case PK							Pallet
Shelf Life: 35 Months Whsl. Code #: Fineline Code: Is Item? Unit Dose Unit of Use If Unit Dose, is item bar coded to unit dose for Hospital tracking purposes? Yes No Will handling data change in the first: 6 months? Yes 9 months? Yes 9 months? Yes 12 months? Yes Unknown? Yes Whsl. Code #: CR Tablets Glass jar Carton: Glass jar Carton: Item: 1 ttem: 3 5215241002 3 Item: 1 ttem: 4 ttem: 4 ttem: 5 7.38" 7.38" 7.31" Item: 1 ttem: 4 Width: 4	•	100/40mg/		Jacob.	10				-	1 -		-	100
Whsl. Code #:	Shelf Life: 35 Months			Carton:									100
Fineline Code: Stem? Unit Dose Unit of Use Item: 3 5215241002 3 1.34 oz 7.31" 1.63" 48"	***************************************		_						_	_	-	g	
Is Item? Unit Dose Unit of Use Unit of Use If Unit Dose, is item bar coded to unit dose for Hospital tracking purposes? Yes No No Will handling data change in the first: 6 months? Yes 9 months? Yes 12 months? Yes Unixown? Yes PPK Unixown? Yes PPK PFK PPK PFK PF			_	Item:			Item:		Width:	Width:	v	/idth:	
If Unit Dose, is item bar coded to unit dose for Hospital tracking purposes? Yes	Fineline Code:			_ 3 5215241002	2 3		1.34 oz		7.31"	1.63"	4	8"	
Iff Unit Dose, is item bar coded to unit dose for Hospital tracking purposes? Yes	Is Item? Unit Dose Unit of Use	For Generic D	rug Product	s: I. Orange	e Book Rat	ing: AB			II. Produ	ct Color: ye	ellow		
COST INFORMATION COST INFORM	•						ontinr					Oxycodone	CR Tablet
Will handling data change in the first: Regular Cost (\$) Purchase Allowance Distribution Allowance Cost (\$) Regular Cost (\$) Price (\$) AWP Price (\$) Furchase Allowance Cost (COST	INFORM	ATION					
6 months?	☐ Yes ☐ No			Purchase Allo	wance [Distribution Al	lowance	Invoice	Net	Mfr's	Avg Ret	I SRP	Excise
9 months?	_			OI	BB	□ OI □	BB	Cost (\$)	Cost (\$)	AWP	Price (\$) (\$)	Tax
12 months?			(\$)	\$	% 5	\$	%						
Unknown? Yes PPK	Name of the state							\$519.33		\$622.25			
omnown. Lites								ψυ10.33		ΨULL.LU			
	Issuet		nin to all a st	llaral assessed	to oo	ماداد ماداد		ni	atura-	<u> </u>	ı	1	

Copyright © 2005 by the Healthcare Distribution Management Association

Revised 02/21/06

Tabulational Information is necessary, provide on right of page or as attachment. Stins product. Stins product. Yes No No No No No No No N	Item Description: Oxycodone CR Tablets	3	Manufacturer: Actavis Totowa LLC
Set his product: a) Cytodoxic?	If additional information is necessary, provide on righ	t of page or as attachment.	
a) Cytotoxic?		NFORMATION	ADDITIONAL INFORMATION AS NECESSARY
Is this item an aerosol requiring special clean-up instructions? Yes No Does this product require special clean-up instructions? Yes No If yes, attach MSDS with special instructions. Department of Transportation (DOT) I.D. Number:	a) Cytotoxic? ☐ Yes ☒ No b) Carcinogen? ☐ Yes ☒ No c) Inhalation Hazard? ☐ Yes ☒ No		
Does this product require special clean-up instructions? Yes No If yee, attach MSDS with special instructions. Department of Transportation (DOT) I.D. Number: Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. Hazard Class(s) for this product Class Hazard Class(s) for this product Class Hazard Class(s) for this product Class Hazard Class(s) for this product Passenger & Cargo Hazard Class(s) for this product Passenger & Cargo Hazard Class(s) for all shipping? Hazard Class(s) for all shipping recurrence Hazard Class(s) for this product for be shipped to customers on dry ice? Yes No Hosping for as an attachment. Hazard Class Hazar	Is this item considered a carcinogen?	☐ Yes	
If yes, attach MSDS with special instructions. Department of Transportation (DOT) LD. Number: Hazard Class/GM Code: OSHA/DOT CHEMICAL_STORAGE CLASS Please check appropriate Class(s) for this product. Ø ORGANIC ANTINEOPLASTIC	Is this item an aerosol requiring special storage?	☐ Yes	
Department of Transportation (DOT) I.D. Number: Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. SORGANIC ANTINEOPLASTIC STEROID/ANDROGEN INORGANIC INORGANI	Does this product require special clean-up instruction	ns? ☐ Yes ☒ No	
Hazard Class/ORM Code: OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. ORGANIC STEROID/ANDROGEN NORGANIC STEROID/ANDROGEN CORROSIVE/OXIDIZER ESSENTIAL CHEMICAL AEROSOL PRECURSOR CHEMICAL (Describe below) AEROSOL PRECURSOR CHEMICAL (Describe below) AEROSOL CLASS MAXIMUM QTY LEVEL Is the product restricted for air shipping? Cargo Passenger Cargo Passenger & Cargo Precursor Chemical: Size/Strength Ephedrine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Sthis product to be shipped to customers on lice? Yes No Is this product to be shipped to customers on dry ice? Yes No Is this product tequire refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	If yes, attach MSDS with special instructions		
OSHA/DOT CHEMICAL STORAGE CLASS Please check appropriate Class(s) for this product. SORGANIC ANTINEOPLASTIC INORGANIC STEROID/ANDROGEN CORROSIVE/OXIDIZER ESSENTIAL CHEMICAL AEROSOL PRECURSOR CHEMICAL (Describe below) AEROSOL ARXIMUM GTY LEVEL Is the product restricted for air shipping? Passenger Cargo Passenger & Cargo Precursor Chemical: Size/Strength Ephedrine Yes No Pseudoephedrine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Sthis product to be shipped to customers on ice? Yes No Is this product tequire refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If Yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	Department of Transportation (DOT) I.D. Number:		
Please check appropriate Class(s) for this product. ORGANIC	Hazard Class/ORM Code:		
ORGANIC	OSHA/DOT CHEMICAL STO	DRAGE CLASS	
INORGANIC STEROID/ANDROGEN CORROSIVE/OXIDIZER ESSENTIAL CHEMICAL DESCRIBE BEIOW	Please check appropriate Class(s) for this product.		
CORROSIVE/OXIDIZER ESSENTIAL CHEMICAL Chescribe below AEROSOL PRECURSOR CHEMICAL (Describe below) AEROSOL CLASS MAXIMUM QTY LEVEL Is the product restricted for air shipping? Passenger Cargo Passenger & Cargo Precursor Chemical: Size/Strength Ephedrine Yes No Pseudoephedrine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No St this product to be shipped to customers on ice? Yes No Does this product require refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	☑ ORGANIC ☐ ANTINEOPLASTIC		
AEROSOL PRECURSOR CHEMICAL (Describe below) AEROSOL CLASS MAXIMUM QTY LEVEL Is the product restricted for air shipping? Passenger Cargo Passenger & No Pasudoephedrine Yes No Pasudoep	☐ INORGANIC ☐ STEROID/ANDROGEN		
AEROSOL CLASS MAXIMUM QTY LEVEL	☐ CORROSIVE/OXIDIZER ☐ ESSENTIAL CHEMICAL	-	
Is the product restricted for air shipping? Passenger Cargo Passenger & Cargo Passenger & Cargo Passenger & Cargo Precursor Chemical: Size/Strength Ephedrine Yes No Pseudoephedrine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Is this product to be shipped to customers on ice? Yes No Is this product to be shipped to customers on dry ice? Yes No Is this product require refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	☐ AEROSOL ☐ PRECURSOR CHEMICA	AL (Describe below)	
Passenger Cargo Passenger & Cargo Precursor Chemical: Size/Strength Ephedrine Yes No Pseudoephedrine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Pseudoephedrine Yes No Phenylpropanolamine Yes No Pseudoephedrine Yes Yes No Pseudoephedrine			
Precursor Chemical: Ephedrine Pseudoephedrine Pseudophedrine Phenylpropanolamine Phenylpropanolamine Pyes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Phenylpropanolamine Yes No Striss product to be shipped to customers on ice? Yes No Is this product to be shipped to customers on dry ice? Yes No Does this product require refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	☐ Passenger		
Precursor Chemical: Ephedrine Yes No Pseudoephedrine Yes No Phenylpropanolamine ADDITIONAL STORAGE AND SHIPPING REQUIREMENTS Is this product to be shipped to customers on ice? Is this product to be shipped to customers on dry ice? Yes No Is this product require refrigerated truck for transport? Is this Product State Regulated? If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No	_		
Ephedrine		Siza/Strangth	
Pseudoephedrine		_	
ADDITIONAL STORAGE AND SHIPPING REQUIREMENTS Is this product to be shipped to customers on ice? Yes No Is this product to be shipped to customers on dry ice? Yes No Does this product require refrigerated truck for transport? Yes No Is this Product State Regulated? Yes No If yes, list states on the right or as an attachment. Are there special returns requirements? Yes No			
Is this product to be shipped to customers on ice?	Phenylpropanolamine 🗌 Yes 🛛 N	o	
Is this product to be shipped to customers on ice?	ADDITIONAL STORAGE AND SHIP	PING REQUIREMENTS	
Does this product require refrigerated truck for transport? ☐ Yes ☐ No Is this Product State Regulated? ☐ Yes ☐ No If yes, list states on the right or as an attachment. Are there special returns requirements? ☐ Yes ☐ No			
Is this Product State Regulated?	Is this product to be shipped to customers on dry ice?	? ☐ Yes	
If yes, list states on the right or as an attachment. Are there special returns requirements? ☐ Yes ☒ No	Does this product require refrigerated truck for transp	oort? ☐ Yes	
	_		
If yes, provide requirements in the space to the right or as attachment.	Are there special returns requirements?	☐ Yes	
	If yes, provide requirements in the space to t	he right or as attachment.	

Now... more choices for pain management.



Oxycodone Hydrochloride Controlled-release Tablets, available from Actavis.

- Compare to OxyContin®*
- Dosage strengths of 10 mg, 20 mg, 40 mg and 80 mg
- 100-count bottles
- Another controlled-release product in our portfolio

To learn more, contact your Actavis representative or wholesaler, or call customer service at 888.925.2342.

Product	Strength	Size	NDC#
Oxycodone HCl CR Tablets	10 mg	100	52152-408-02
Oxycodone HCl CR Tablets	20 mg	100	52152-409-02
Oxycodone HCl CR Tablets	40 mg	100	52152-410-02
Oxycodone HCl CR Tablets	80 mg	100	52152-411-02

Please see adjacent pages for prescribing information.

A260 Rev. 9/2009

*OxyContin® is the registered trademark of Purdue Pharma L.P.



OXYCODONE HCI CONTROLLED-RELEASE TABLETS

10 mg, 20 mg, 40 mg, 80 mg* R_x Only

*80 mg, and 160 mg is for use in opioid-tolerant patients only

Oxycodone HCl Controlled-Release Tablets are an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

Oxycodone can be abused in a manner similar to other opioid agonists, legal Oxycoacute can be audused in a manner similiar to other opioid agoints, regal or illicit. This should be considered when prescribing or dispensing Oxycodone HCI Controlled-Release Tablets in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Oxycodone HCI Controlled-Release Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

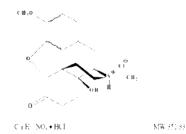
Oxycodone HCl Controlled-Release Tablets are NOT intended for use as a

OXYCODONE HCI CONTROLLED-RELEASE 80 mg, and 160 mg Tablets, or a single dose greater than 40 mg, ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids.

OXYCODONE HCI CONTROLLED-RELEASE TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED DXYCODONE HCI CONTROLLED-RELEASE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

DESCRIPTION

Oxycodone NCI Controlled-Release Tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths for oral administration. The tablet strengths describe the amount of govçodone per tablet as the hydrochloride salt. The structural formula for oxycodone hydrochloride is as follows:



The chemical formula is 4, 5a-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one

Oxycodone is a white, odorless crystalline powder derived from the opium alkaloid, thebaine. Oxycodone hydrochloride dissolves in water (1 g in 6 to 7 mt.). It is slightly soluble in alcohol (octanol water partition coefficient 0.7). The tablets contain the following inactive ingredients: ammonio methacylate copolymer, hypromellose, lactose, magnesium stearate, polyethylene glycol 400, povidone, sodium hydroxide, sorbic acid, stearyl alcohol, talc, titanium dioxide, and traretrin

The 10 mg tablets also contain: hydroxypropyl cellulose.

The 20 mg tablets also contain: polysorbate 80 and red iron oxide

The 40 mg tablets also contain: polysorbate 80 and yellow iron oxide

The 80 mg tablets also contain: FD&C blue No. 2, hydroxypropyl cellulose, and yellow iron oxide.

Oxycodone HCI controlled-release 10 mg, 20 mg, 40 mg, and 80 mg tablets are tested using USP Dissolution Test 2 and meet the associated tolerances provided in Acceptance Table 2 of the Oxycodone Hydrochloride Extended-Release Tablets USP Monograph.

CLINICAL PHARMACOLOGY

CLINICAL PHARMACOLOGY
Obycodone is a pure agonist opioid whose principal therapeutic action is analgesia. Other members of the class known as opioid agonists include substances such as morphine, hydromorphone, fentanyl, codeine, and hydrocodone. Pharmacological effects of policid agonists include analolysis, euphoria, feelings of relaxation, respiratory depression, constipation, moiss, and cough supports and sevel glas analgesia. Like all pure opioid agonists, and supports and sevel as analgesia, utilike with mixed agonist/ antagonists or non-poid analgesics, where there is a limit to the analgesic effect which increasing doses. With pure opioid agonist analgesics, there is a limit to the analgesic effect with increasing doses. With pure opioid agonist analgesics, there is no defined maximum dose; the ceiling to analgesic effectiveness is imposed only by side effects, the more serious of which may include somnolence and respiratory depression.

Central Nervous System
The precise mechanism of the analgesic action is unknown. However, specific CNS opioid
receptors for endogenous compounds with opioid-like activity have been identified
throughout the brain and spinal cord and play a role in the analgesic effects of this drug.

Oxycodone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves both a reduction in the responsiveness of the brain stem respiratory centers to increases in carbon dioxide tension and to electrical stimulation.

Oxycodone depresses the cough reflex by direct effect on the cough center in the medulla. Antitussive effects may occur with doses lower than those usually required for analgesia.

Oxycodone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origin may produce sminal findings). Market mydrialsis rather than miosis may be seen with hypoxia in the setting of Oxycodone HCI Controlled-Release Tablets overdose (See OVERDOSAGE).

Gastrointestinal Tract And Other Smooth Muscle

Objective Test And Unter Smooth Muscle
Oxycodine causes a reduction in motility associated with an increase in smooth muscle tone in
the antum of the stomach and duodenum. Digestion of food in the small intestine is delayed
and propulsive contractions are decreased. Propulsive peristatic waves in the color
and corrected, while tone may be increased to the point of spasm resulting in constipation. Other
opioid-induced effects may include a reduction in gastric, billary and pancreatic secretions,
spasm of sphincter of Oddi, and transient elevations in serum amylase.

Cardiovascular System
Osycodone may produce release of histamine with or without associated peripheral vasodilation. Mainfestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or orthostatic hypotension.

CII

Concentration – Efficacy Relationships
Studies in normal volunteers and patients reveal predictable relationships between oxycodon dosage and plasma oxycodon concentrations, as well as between concentration and certain expected opioid effects, such as pupillary constriction, sedation, overall "drug effect," analgesis and feelings of "relaxation."

As with all opioids, the minimum effective plasma concentration for analgesia will vary widely As with a judgment, septically applied to the control to the contr

Concentration – Adverse Experience Relationships
Oxycodone HCI Controlled-Release Tablets are associated with typical opioid-related adverse experiences. There is a general relationship between increasing oxycodone plasma concentration and increasing frequency of dose-related opioid adverse experiences such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation is altered by the development of tolerance to opioid-related side effects, and the relationship is not clinically relevant.

As with all opioids, the dose must be individualized (see **DOSAGE AND ADMINISTRATION**), because the effective analgesic dose for some patients will be too high to be tolerated by other patients.

PHARMACOKINETICS AND METABOLISM

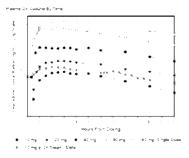
Breaking, chewing or crushing Oxycodone HCI Controlled-Release Tablets eli-controlled delivery mechanism and results in the rapid release and absorption of

tatal once of oxyconone.

Oxycodone Telases from Oxycodone HCI Controlled-Release Tablets is pH independent.
Oxycodone lesses from Oxycodone HCI Controlled-Release Tablets with an oral bioavailability of Oxycodone HCI Controlled-Release Tablets with an oral bioavailability of Oxycodone HCI Controlled-Release Tablets in Immediate-release or all obases form is 100%. Upon repeated dosing in normal volunteers in pharmacokinetic studies, steady-state levels were achieved within 24 hours. Do the proportionality and/or bioavailability has been established for the 10 mg, 20 mg, 80 mg, and 160 mg tablet strengths for both peak plasma levels (C_{ma}) and extent of absorption (AUC). Oxycodone is extensively metabolites. The apparent eliminated primarily in the urine as both conjugated and unconjugated metabolites. The apparent elimination half-life of oxycodone following the administration of Oxycodone HCI Controlled-Release Tablets was 4.5 hours compared to 3.2 hours for immediate-release oxycodone.

Absorption
About 60% to 67% of an oral dose of oxycodone reaches the central compartment in comparison to a parenteral dose. This high oral bloavailability is due to low pre-systemic and/or first-pass metabolism. In normal volunteers, the 1½ of absorption is 0.4 hours for immediate-release oral oxycodone. In contrast, Oxycodone HC Controlled-Release Tablets exhibit a biphasic absorption pattern with two apparent absorption half-lives of 0.6 and 6.9 hours, which describes the initial release of oxycodone from the tablet followed by a prolonged

Plasma Oxycodone by Time
Dose proportionality has been established for the 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths for both peak plasma concentrations (C_{ma}) and extent of absorption (AUC) (see Tablet 1 below). Another study established that the 160 mg tablet is bioequivalent to 2 x 80 mg tablets as well as to 4 x 40 mg for both peak plasma concentrations (C_{ma}) and extent of absorption (AUC) (see Table 2 below), Geen the short Intal-fiel of elimination of oxycodone from Oxycodone HCI Controlled-Release Tablets, steady-state plasma concentrations of oxycodone are achieved within 24-36 hours of initiation of dosing with Oxycodone HCI Controlled-Release Tablets. In a study comparing 10 mg of Oxycodone HCI Controlled-Release Tablets every 12 hours to 5 mg of immediate-release oxycodone every 6 hours, the two treatments were found to be equivalent for AUC and C_{max}, and similar for C_{max} (trough) concentrations.



Mean [% coefficient variation]

Regilileil/	Dosage roili	AUC (ng-hr/mL)†	C _{max} (ng/mL)	T _{max} (hrs)	Conc. (ng/mL)	
Single Dose	10 mg Oxycodone HCl Controlled- Release Tablets	100.7 [26.6]	10.6 [20.1]	2.7 [44.1]	n.a.	
	20 mg Oxycodone HCl Controlled- Release Tablets	207.5 [35.9]	21.4 [36.6]	3.2 [57.9]	n.a.	
	40 mg Oxycodone HCl Controlled- Release Tablets	423.1 [33.3]	39.3 [34.0]	3.1 [77.4]	n.a.	
	80 mg Oxycodone HCl Controlled- Release Tablets*	1085.5 [32.3]	98.5 [32.1]	2.1 [52.3]	n.a.	
Multiple Dose	10 mg Oxycodone HCl Controlled- Release Tablets Tablets q12h	103.6 [38.6]	15.1 [31.0]	3.2 [69.5]	7.2 [48.1]	
	5 mg immediate- release q6h	99.0 [36.2]	15.5 [28.8]	1.6 [49.7]	7.4 [50.9]	

Table 2 Mean [% coefficient variation]

Regimen/	Dosage Form	AUC∞ (ng•hr/mL)‡	C _{max} (ng/mL)	T _{max} (hrs)	Trough Conc. (ng/mL)
Single Dose	4 x 40 mg Oxycodone HCl Controlled- Release Tablets*	1935.3 [34.7]	152.0 [28.9]	2.56 [42.3]	n.a.
	2 x 80 mg Oxycodone HCl Controlled- Release Tablets*	1859.3 [30.1]	153.4 [25.1]	2.78 [69.3]	n,a.
	1 x 160 mg Oxycodone HCI Controlled- Release Tablets*	1856.4 [30.5]	156.4 [24.8]	2.54 [36.4]	n,a.

† for single-dose AUC = AUC_{out} for multiple-dose AUC = AUC_{o-1}
* data obtained while volunteers received naltrexone which can enhance absorption

Oxycodone HCI Controlled-Release Tablets are NOT INDICATED FOR RECTAL ADMINISTRATION. Data from a study involving 21 normal volunteers show that Oxycodone HCI Controlled-Release Tablets administered per rectum resulted in an AUC 39% greater and a $\alpha_{\rm max}$.9% higher than tablets administered by mouth. Therefore, there is an increased risk of adverse events with rectal administration.

Food Effects

FOOD ETHERS. Food has no significant effect on the extent of absorption of oxycodone from Oxycodone HCI Controlled-Release Tablets. However, the peak plasma concentration of oxycodone increased by 25% when an Oxycodone HCI Controlled-Release Tablets 160 mg Tablet was administered with a high-fat meal.

Distribution

Following intravenous administration, the volume of distribution (Vss) for oxycodone was 2.6. L/kg. Oxycodone binding to plasma protein at 37°C and a pH of 7.4 was about 45%. Once absorbed, oxycodone is distributed to skeletal muscle, liver, intestinal tract, lungs, spleen, and brain. Oxycodone has been found in breast milk (see PRECAUTIONS).

Metabolism

Dsycodone hydrochloride is extensively metabolized to noroxycodone, oxymorphone, noroxymorphone, and their glucuronides. The major circulating metabolite is noroxycodone with an AUC ratio of 0.6 relative to that of oxycodone. Noroxycodone is reported to be a considerably weaker analgesic than oxycodone. Oxymorphone, although possering analgesic activity, is present in the plasma only in low concentrations. The correlation between oxymorphone concentrations and opicid effects was much less than that seem with oxycodone plasma concentrations. The analgesic activity profile of other metabolities is not known.

The formation of oxymorphone and noroxycodone, is mediated by cytochrome P450 2D6 and cytochrome P450 3A4, respectively. In addition, noroxymorphone formation is mediated by both cytochrome P450 D8 and cytochrome P450 3D8 and cytochrome P450 3D8 and cytochrome P450 D8 and cytochrome P450 3D8 and cytochrome P450 3D8 and cytochrome P450 3D8 and cytochrome P450 B8 and

Excretion

Oxycodone and its metabolites are excreted primarily via the kidney. The amounts measured in the urine have been reported as follows: free oxycodone up to 19%; conjugated oxycodone up to 50%; free oxymorphone 0%; conjugated oxymorphone s 14%; both free and conjugated noroxycodone have been found in the utrine but not quantified. The total plasma clearance was 0.8 L/min for adults.

Special Populations

The plasma concentrations of oxycodone are only nominally affected by age, being 15% greater in elderly as compared to young subjects.

Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis. The reason for this difference is unknown.

Renal impairment
Data from a pharmacokinetic study involving 13 patients with mild to severe renal dysfunction (creatinine clearance <60 ml/min) show peak plasma oxyrodone and noroxycodone concentrations 50% and 20% higher, respectively, and AUC values for oxycodone, protocodone, and oxymorphone 60%, 50%, and 40% higher than normal subjects, respectively. This is accompanied by an increase in sedation but not by differences in respiratory rate, pupillary constriction, or several other measures of drug effect. There was an increase in the of elimination for oxycodone of only 1 hour (see PRECAUTIONS).

Hepatic Impairment

inepaux impairment
Data from a tudy implaining 24 patients with mild to moderate hepatic dysfunction show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, than normal relects and 40% uses are 5% and 65% higher respectively. Oxymorphone peak plasma normal relects and 40% uses are 5% and 65% higher respectively. Oxymorphone peak plasma oxymorphone and 40% peak plasma oxymorphone oxymorp

Drug-Drug Interactions (see PRECAUTIONS)Oxycodone is metabolized in part by cytochrome P450 2D6 and cytochrome P450 3A4 and in theory can be affected by other drugs.

Oxycodone is metabolized in part by cytochrome P450 2D6 to oxymorphone which represents less than 15% of the total administreed dose. This route of elimination may be blocked by a variety of drugs [e.g., certain cardiovascular drugs including amiodiaone and quintidine as well as polycyclic arti-depressants). However, in a study involving 10 subjects using quintidine, a known inhibitor of cytochrome P450 2D6, the pharmacodynamic refers of oxycodome were unchanged.

Pharmacodynamics

Praarmaccog/namics
A single-dose, double-blind, placebo- and dose-controlled study was conducted using Oxycodone HCl Controlled-Release Tablets (10, 20, and 30 mg) in an analgesic pain model involving 182 paients with moderate to severe pain. Twenty and 30 mg of Oxycodone HCl Controlled-Release Tablets were superior in reducing pain compared with placebo, and this difference was statistically significant. The onset of analgesic action with Oxycodone HCl Controlled-Release Tablets occurred within 1 hour in most patients following oral administration

CLINICAL TRIALS

CLINICAL HALS

A double-blind placebo-controlled, fixed-dose, parallel group, two-week study was conducted in 133 patients with chronic, moderet be severe pain, who were judged as having linadequate pain control with their current theory. In this study, 20 mg Gyvocdone HC Gontrolled-Felesae Tablets q12h durt or 10 mg Gycodone HC Controlled-Felesae Tablets q12h decreased pain compared with placebo, and this difference was statistically significant.

INDICATIONS AND USAGE

INDICATIONS AND OSAGE
Oxycodone HCI Controlled-Release Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

Oxycodone HCl Controlled-Release Tablets are NOT intended for use as a prn analgesis

Physicians should individualize treatment in every case, initiating therapy at the appropriate point along a progression from non-opioid analgesics, such as non-steroidal anti-inflammatory drugs and actariamophen to opioids in a plan of plan management such as outlined by World Health Organization, the Agency for Health care Policy and Research), the Federation of State Medical Boards Model Guidelines, or the American Pain Society.

Oxycodone HCI Controlled Release Tablets are not indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild, or not expected to persist for an extended period of time. Oxycodone HCI Controlled Release Tablets are only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

CONTRAINDICATIONS
Oxycodone HCI Controlled-Release Tablets are contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercarbia. Oxycodone HCI Controlled-Release Tablets are contraindicated in any patient who has or is suspected of having paralytic ileus.

WARNINGS

OXYCODONE NEIC CONTROLLED-RELEASE TABLETS ARE TO BE SWALLOWED WHOLE AND ABE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OXYCODONE HCI CONTROLLED-RELEASE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

Oxycodone HCI Controlled-Release 80 mg Tablets, or a single dose greater than 40 mg. ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. A single dose greater than 40 mg. or total daily doses greater than 80 mg. may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of

Oxycodone HCI Controlled-Release 80 mg Tablets are for use only in opioid-tolerant patients requiring daily oxycodone equivalent dosages of 160 mg or more. Care should be taken in the prescribing of this tablet strength. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

Misuse, Abuse and Diversion of Opioids

Oxycodone is an opioid agonist of the morphine-type. Such drugs are sought by drug abusers and people with addiction disorders and are subject to criminal diversion.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Oxycodone HCI Controlled-Release Tablets in situations where the physician or pharmacist is concerned about an increased risk of misus, abuse, or diversion.

Oxycodone HCI Controlled-Release Tablets have been reported as being abused by crushing, chewing, snorting, or injecting the dissolved product. These practices will result in the uncontrolled delivery of the opioid and pose a significant tick to the abuser that could result in overdose and death (see WARNINGS and DRUG ABUSE AND ADDICTION).

Concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

Healthcare professionals should contact their State Professional Licensing Board, or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.

Interactions with Alcohol and Drugs of Abuse
Oxycodone may be expected to have additive effects when used in conjunction with alcohol,
other opioids, or illicit drugs that cause central nervous system depression.

DRUG ABUSE AND ADDICTION
Oxycodone HCI Controlled-Release Tablets contain oxycodone which is a full muagonist opioid with an abuse ilability similar to morphine and is a Schedule II
controlled substance. Oxycodone, like morphine and other opioids used in analgesia,
can be abused and is subject to criminal diversion.

Drug addiction is characterized by compulsive use, use for non-medical purposes, and continued use despite harm or risk of harm. There is a potential for drug addiction to develop following exposine to opioids, including oxycodome. Drug addiction is a treatable disease, utilizing a multi-disciplinary approach, but relapse is common.

"Drug-seeking" behavior is very common in addicts and drug abusers. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing or referral, repeated "loss" of prescriptions, tampering with prescriptions and reluctance to provide prior medical records or contact information for other treating physician(s). "Doctor shopping" to obtain additional prescriptions is common among drug abusers and people suffering from untreated addiction

Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction and is characterized by misuse for non-medical purposes, often in combination with other psychoactive substances. Oxycodone HIC controlled-Release Tablets, like other opioids, have been diverted for non-medical use. Careful record-been diverted for non-medical use. Careful record-been diverted for non-medical use. Careful record-been diverted for non-medical use.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Oxycodone HCl Controlled-Release Tablets consist of a dual-polymer matrix, intended Oxycotone net Controllee-Release lablets consist of a dual-polymer matrix, intended for oral use only. Abuse of the crushed tablet poses a hazard of overdose and death. This risk is increased with concurrent abuse of alcohol and other substances. With parenteral abuse, the tablet excipients, especially talc, can be expected to result in local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valualar heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases such as hepatitis and HIV.

Respiratory Depression

Respiratory depression is the chief hazard from oxycodone, the active ingredient in Oxycodone HCL Controlled-Release Tablets, as with all opioid agonists. Respiratory depression is a particular problem in elderly or debilitated patients, usually following large initial does in non-tolerant patients, or when opioids are given in conjunction with other agents that depress

Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression, in such patients, vere usual threapeuti doses of oxycodone may decrease respiratory dive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

Head in Jury
The respiratory depressant effects of opioids include carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure, and may be markedly exaggerated in the presence of head injury, intracrianal lecisions, or other sources of pre-existing increased intracranial pressure. Oxycodone produces effects on pupillary response and consciousness which may obscure neurologic signs of further increases in intracranial pressure in patients with head injuries.

Hypotensive Effect
Oxycodone HCI Controlled-Release Tablets may cause severe hypotension. There is an added
six to individuals whose ability to maintain blood pressure has been compromised by a
depleted blood volume, or after concurrent administration with drugs such as phenothiazines or other agents which compromise vasomotor tone. Oxycodone may produce orthor bypotension in ambulatory patients, Oxycodone, like all opioid analgesics of the more type, should be administered with caution to patients in circulatory shock, since vasodi produced by the drug may further reduce cardiac output and blood pressure.

Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined with CNS depressant drugs, and should be reserved for cases where the benefits of goidol analgesia outwelpth the known risks of respiratory depression, altered mental state, and postural hypotension.

Use of Dxycodone HCI Controlled-Release Tablets is associated with increased potential risks and should be used only with caution in the following conditions: acute alcohollsin; adrenocortical insufficiency (e.g., Addisions disease); CNS depression or coma; definition themes; debitdad patients, kyphoscoliosis associated with respiratory depression; myxedema or hypothyroidism; prostatic hypertrolly or urefula fixtrue; severe impairment of hepatic, builmonary or renal more controlled to the controlled or controlled to the controlled or controll

The administration of oxycodone may obscure the diagnosis or clinical course in patients with acute abdominal conditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

Interactions with other CNS Depressants

Interactions with other LNS Depressants
Opygodone HG Controlled-Release Tablets should be used with caution and started in a
reduced dosage (1/3 to 1/2 of the usual dosage) in patients who are concurrently receiving
other central nervous system depressants funding sedatives or hypnotics, general anesthetics,
phenothiazines, other tranquilizers, and alcohol. Interactive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result if these drugs are taken in combination with the usual doses of Oxycodone HCl Controlled-Release Tablets.

Interactions with Mixed Agonist/Antagonist Opioid Analgesics Agonist/Antagonist analgesics (i.e., pentazorine, nalbuphine, and butorphanol) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as oxycodone. In this situation, mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and/or may precipitate withdrawal symptoms in these patients.

Ambulatory Surgery and Postoperative Use
Oxycodone HCl Controlled-Release Tablets are not indicated for pre-emptive analgesia (administration pre-operatively for the management of postoperative pain).

Oxycodone HCl Controlled-Release Tablets are not indicated for pain in the immedia postoperative period (the first 12 to 24 hours following surgery) for patients is previously taking the drug, because its safety in this setting has not been established

Oxycodone HCl Controlled-Release Tablets are not indicated for pain in the postop period if the pain is mild or not expected to persist for an extended period of tim

Oxycodone HCI Controlled Release Tablets are only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time Physician's should individualize treatment, moving from parenteral to oral analgesics as appropriate (See American Pain Society guidelines).

Patients who are already receiving Oxycodone HCl Controlled-Release Tablets as part of ongoing analgesic therapy may be safely continued on the drug if appropriate dosage adjustments are made considering the procedure, other drugs given, and the temporary changes in physiology caused by the surgical intervention (see **DOSAGE AND ADMINISTRATION**).

Oxycodone HCI Controlled-Release Tablets and other morphine-like opioids have been shown to decrease bowel motility. Ilsus is a common postoperative complication, especially after intra-abdominal surgery with opioid analgesia. Caution should be taken to monitor for decreased bowel motility in postoperative patients receiving opioids. Standard supportive therapy should be implemented.

Use in Pancreatic/Billiary Tract Disease
Oxycodone may cause spasm of the sphincter of Oddi and should be used with caution in
patients with bilary tract disease, including acute pancreatitis. Opioids like oxycodone may
cause increases in the serum amylase level.

Tolerance and Physical Dependence

Tolerance and PTYSIGL Dependence following is the need for increasing does of opioids to maintain a defined effect such as analyseia (in the absence of disease progression or other external factors). Polysical dependence is manifested by withdrawal symptoms after abrupt obscribing or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.

The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other symptoms abo may develop, including: irraibility, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomitting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

In general, opioids should not be abruptly discontinued (see DOSAGE AND ADMINISTRATION: Cessation of Therapy).

Information for Patients/Caregivers

If clinically advisable, patients receiving Oxycodone HCI Controlled-Release Tablets or their caregivers should be given the following information by the physician, nurse, pharmacist, or caregiver.

1. Patients should be aware that Oxycodone HCI Controlled-Release Tablets contain oxycodone, which is a morphine-like substance.

Patients should be advised that Oxycodone HCI Controlled-Release Tablets were designed to work properly only if swallowed whole. Oxycodone HCI Controlled-Release Tablets will release all their contents at once if broken, chewed, or crushed, resulting in a risk of fatal overdose.

3. Patients should be advised to report episodes of breakthrough pain and adverse experiences occurring during therapy. Individualization of dosage is essential to make optimal use of this

4. Patients should be advised not to adjust the dose of Oxycodone HCl Controlled-Release Tablets without consulting the prescribing professional.

5. Patients should be advised that Oxycodone HCI Controlled-Release Tablets may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating heavy machinery).

6. Patients should not combine Oxycodone HCI Controlled-Release Tablets with alcohol or other central nervous system depressants (sleep aids, tranquilizers) except by the orders of the prescribing physician, because dangerous additive effects may occur, resulting in serious

7. Women of childbearing potential who become, or are planning to become, pregnant should be advised to consult their physician regarding the effects of analgesics and other drug use during pregnancy on themselves and their unborn child.

8. Patients should be advised that Oxycodone HCI Controlled-Release Tablets are a potential drug of abuse. They should protect it from theft, and it should never be given to anyone other than the individual for whom it was prescribed.

9. Patients should be advised that they may pass empty matrix "ghosts" (tablets) via colostomy or in the stool, and that this is of no concern since the active medication has already been

10. Patients should be advised that if they have been receiving treatment with Oxycodone HCI To, reatives should be advised that it duey nave been receiving reastment with oxylocutine Activities of Controlled -Release Tablets for more than a few weeks and cessation of therapy is indicated, it may be appropriate to taper the Oxycodone HCI Controlled-Release Tablets does, rather than abruptly discontinue; it, due to the risk of precipitating withdrawal Symptoms. Their physician can provide a dose schedule to accomplish a gradual discontinuation of the medication.

11. Patients should be instructed to keep Oxycodone HCl Controlled-Release Tablets in a secure place out of the reach of children. When Oxycodone HCl Controlled-Release Tablets are no longer needed, the unused tablets should be destroyed by flushing down the toilet.

Use in Drug and Alcohol Addiction
Osycodone HCI Controlled-Release Tablets are an opioid with no approved us
management of addictive disorders. Its proper usage in individuals with drug or
dependence, either active or in remission, is for the management of pain requirin

Drug-Drug InteractionsOpioid analgesics, including Oxycodone HCI Controlled-Release Tablets, may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory degression.

Oxycodone is metabolized in part by cytochrome P450 2D6 and cytochrome P450 3A4 and in theory can be affected by other drugs

Oxycodone is metabolized in part to oxymorphone via cytochrome P450 2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs including amiodarone and quinidine as well as polycyclic antidepressantly, such blockade has not yet been shown to be of clinical significance with this agent. Clinicians should be aware of this possible interaction, however.

Use with CNS Depressants
Oxycodone HCI Controlled-Release Tablets, like all opioid analgesics, should be started at 1/3 to 1/2 of the sural dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothilazines, centrally acting anti-emetics, tranquilizers, and altohol because respiratory depression, hypotension, and profound sedation or coma may result. No specific interaction between oxycodone and monoamine coidages inhibitors has been observed, but caution in the use of any opioid in patients taking this class of drugs is appropriate.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies of oxycodone to evaluate its carcinogenic potential have not been conducted.

Oxycodone was not mutagenic in the following assays: Ames Salmonella and E. coli test with and without metabolic activation at doses of up to 5000 µg, chromosomal aberation test in human lymphocytes in the absence of metabolic activation at doses of up to 1500 µg/ml and with activation 48 hours after exposure at doses of up to 1600 µg/ml, and in the invivo bone marrow micronucleus test in mixe (at plasma levels of up to 48 µg/ml). Oxycodone was clastogenic in the human phinpocyte chromosomal assay in the presence of metabolic activation in the human chromosomal aberation test (at greater than or equal to 1250 µg/ml, or at 24 but not 48 hours of exposure and in the mouse hymphoma assay at doses of 50 µg/ml, or greater with metabolic activation and at 400 µg/ml. or greater without metabolic activation.

Pregnancy
Ferotagenic Effects - Category B: Reproduction studies have been performed in rats and rabbits by oral administration at doses up to 8 mg/kg and 125 mg/kg, respectively. These doses are 3 and 46 times a human dose of 168 mg/kgb, based on mg/kg basis. The results did not not administration of the results did not not only did pass, the results did not not controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery
Doycodone HCI Controlled-Release Tablets are not recommended for use in women during and
immediately prior to labor and delivery because oral opioids may cause respiratory depression
in the newborn. Neonates whose mothers have been taking oxycodone chronically may exhibit
respiratory depression and/or withdrawal symptoms, either at birth and/or in the nursery.

Nursina Mothers

Low concentrations of oxycodone have been detected in breast milk. Withdrawal symptoms can occur in breast-feeding infants when maternal administration of an opioid analgest is stopped. Ordinantly, runsing should not be undertaken while a patient is receiving Oxycodone HCI Controlled Release Tablets because of the possibility of sedation and/or respiratory depression in the infant.

Pediatric Use
Safety and effectiveness of Oxycodone HCI Controlled-Release Tablets have not been
established in pediatric patients below the age of 18. It must be remembered that Oxycodone
HCI Controlled-Release Tablets cannot be crushed or divided for administration.

Geriatric Use In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone appeared to be slightly reduced. Compared to young adults, the plasmac concentrations of oxycodone were increased approximately 15% less PHARMACOKINET (SAND METABOLISM). Of the total number of subjects (445) in clinical studies of Oxycodone HCI Controlled-Release Tablets, 184 (33.94%) were age 65 and older (Including those agree) and older) while 40 (9.09%) were age 75 and older in clinical trials with appropriate intitation of therapy and dose titration, no untoward or unexpected side effects were seen in the elderly patients who received Oxycodone HCI Controlled-Release Tablets. Thus, the usual doses and patients who received Oxycodone HCL Controlled-Release Tablets. Thus, the usual doses and dosing intervals are appropriate for these patients. As with all opioids, the starting dose should be reduced to 1/3 to 1/2 of the usual dosage in debilitated, non-tolerant patients. Respiratory depression is the chief hazard in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

Laboratory Monitoring
Due to the broad range of plasma concentrations seen in clinical populations, the varying degrees of plasm, and the development of tolerance, plasma oxycodone measurements are usually not helpful in clinical management. Plasma concentrations of the active drug substance may be of value in selected, unusual or complex cases.

Hepatic Impairment
A study of Oxycodone HCI Controlled-Release Tablets in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 1/3 to 1/2 the usual doses and careful dose thration is warranted.

Renal Impairment

nenal impairment in patients with renal impairment, as evidenced by decreased creatinine clearance (<60 mL/ min), the concentrations of oxycodone in the plasma are approximately 50% higher than in subjects with normal renal function. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

Gender Differences

Gender Differences
in pharmacolinet, studies, opioid-naive females demonstrate up to 25% higher average
plasma concentrations and greater frequency of typical opioid adverse events than males,
even after adjustement for dog regist. The clinical relevance of a difference of this magnitude
is low for a drug intended for chronic usage at individualized dosages, and there was no male/
female difference detected for effector, or adverse events in clinical trials.

ADVENSE HEAL TUDE The safety of Dyxpodone HCI Controlled-Release Tablets was evaluated in double-blind clinical trials involving 713 patients with moderate to severe pain of various etiologies. In open-label studies of cancer pain, 187 patients received Dyxpodone HCI Controlled-Release Tablet to total daily doses ranging from 20 mg to 640 mg per day. The average total daily dose was appropriately 105 mg nor day. approximately 105 mg per day.

Serious adverse reactions which may be associated with Oxycodone HCI Controlled-Release Tablet therapy in clinical use are those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, and (to an even lesser degree) circulatory depression, hypotension, or shock (see **OVERDOSAGE**).

The non-serious adverse events seen on initiation of therapy with Oxycodone HCl Controlled-Release Tablets are typical opioid side effects. These events are dose-dependent, and their frequency depends upon the dose, the clinical setting, the patient's level of opioid tolerance, and host factors specific to the individual. They should be expected and managed as a part of opioid analgesia. The most frequent (5-5%) include: constipation, nausea, somnolence, dizzness, womiting, pruntus, headache, dry mouth, sweating, and asthenia.

In many cases the frequency of these events during initiation of therapy may be minimized by careful individualization of starting dosage, alow litration, and the avoidance of large swings in the plasma contentations of the opioid. Many of these adverse events will cease or decrease in intensity as Oxycodone HCI Controlled-Release Tablet therapy is continued and some degree of tolerance is developed.

Clinical trials comparing Oxycodone HCl Controlled-Release Tablets with immediate-re oxycodone and placebo revealed a similar adverse event profile between Oxycodone Controlled-Release Tablets and immediate-release oxycodone. The most common ad events (>5%) reported by patients at least once during therapy were:

Table 3

	Oxycodone HCI Controlled- Release Tablets (n=227)	Immediate-Release (n=225)	Placebo (n=45)
	(%)	(%)	(96)
Constipation	(23)	(26)	(7)
Nausea	(23)	(27)	(11)
Somnolence	(23)	(24)	(4)
Dizziness	(13)	(16)	(9)
Pruritus	(13)	(12)	(2)
Vorniting	(12)	(14)	(7)
Headache	(7)	(8)	(7)
Dry Mouth	(6)	(7)	(2)
Asthenia	(6)	(7)	-
Sweating	(5)	(6)	(2)

The following adverse experiences were reported in Dxycodone HCI Controlled-Release Tablets-treated patients with an incidence between 1% and 5%. In descending order of frequency they were anoreta, nervousness, insomnia, fever, confusion, diarrhea, abdominal pain, dyspepsia, rash, analety, euphoria, dyspinea, postural hypotension, chills, twitching, gastrist, abnormal di derams, thought abnormalities, and hickups.

The following adverse reactions occurred in less than 1% of patients involved in clinical trials or vere reported in postmarketing experienc

Blood and lymphatic system disorders: lymphadenopathy

Cardiac disorders: palpitations (in the context of withdrawal)

Ear and labyrinth disorders: tinnitus

Endocrine disorders: syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Gastrointestinal disorders: dysphagia, eructation, flatulence, gastrointestinal disorder, ileus, increased appetite, stomatitis

General disorders and administration site conditions: chest pain, edema, facial edema, malaise, pain, peripheral edema, thirst, withdrawal syndrome (with and without seizures)

Immune system disorders: anaphylactic or anaphylactoid reaction (symptoms of)

Infections and infestations: pharyngitis

Injury, poisoning and procedural complications: accidental injury

Investigations: hyponatremia, increased hepatic enzymes, ST depression

Metabolism and nutrition disorders: dehydration

Musculoskeletal and connective tissue disorders: neck pain

Nervous system disorders: abnormal gatt, amnesia, hyperkinesia, hypertonia (muscular), hypesthesia, hypotonia, migraine, paresthesia, seizures, speech disorder, stupor, syncope, taste perversion, tremor, vertigo

Psychiatric disorders: agitation, depersonalization, depression, emotional lability, hallucination

Renal and urinary disorders: dysuria, hematuria, polyuria, urinary retention, urination impaired

Reproductive system and breast disorders: amenorrhea, decreased libido, impotence Respiratory, thoracic and mediastinal disorders: cough increased, voice alteration

Skin and subcutaneous tissue disorders: dry skin, exfoliative dermatitis, urticaria

OVERDOSAGE

Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death.

Deaths due to overdose have been reported with abuse and misuse of Oxycodone HCI Controlled-Release Tablets. by ingesting, inhaling, or injecting the crushed tablets. Review of case reports has indicated that the risk of fatal overdose is further increased when Oxycodone HCI Controlled-Release Tablets are abused concurrently with alcohol or other CNS depressants, including other opioids.

In the treatment of oxycodone overdosage, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary eterna uscompanying overdose as indicated. Cardiac arrest or aritythmism says require cardiac massage or deribnilations.

Cardiac artes or armychinas may require cardiac massage or certomicion.
The pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to acycodone overdose. In patients who are physically dependent on any opioid agonist including Oxycodone HCI Controlled-Release Tablets, an abrupt or complete reversal or opioid effects may precipitate an acute abstinence syndrome. The severity of the withdrawal syndrome produced will depend on the degree of physical dependence and the dose of the antagonist administered. Please see the prescribing information for the specific opioid antagonist for details of their proper use.

DOSAGE AND ADMINISTRATION

OXYCODONE HO! CONTROLLED-RELEASE TABLETS ARE AN OPIOID AGONIST AND A SCHEDULE II CONTROLLED SUBSTANCE WITH AN ABUSE LIABILITY SIMILAR TO MORPHINE. OXYCODONE, LIKE MORPHINE AND OTHER OPIOIDS USED IN ANALGESIA, CAN BE ABUSED AND IS SUBJECT TO CRIMINAL DIVERSION.

OXYCODONE HCI CONTROLLED-RELEASE TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OXYCODONE HCI CONTROLLED-RELEASE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

One Oxycodone HCI Controlled-Belease 160 mg tablet is comparable to two 80 mg tablets when taken on an empty stomach. With a high-fat meal, however, there is a 25% greater peak plasma concentration following one 160 mg tablet. Dietary caution should be taken when patients are initially titrated to 160 mg tablets (see DOSAGE AND ADMINISTRATION).

Patients who are not currently taking opioid analgesics should generally be started on the lowest appropriate dose (see DOSAGE AND ADMINISTRATION; Initiation of Therapy).

In treating pain it is vital to assess the patient regularly and systematically. Therapy should also be regularly reviewed and adjusted based upon the patient's own reports of pain and side effects and the health professional's clinical judgment.

emects and the neatin prioressionals clinical judgment.

Oxycodone It/C Ontrolled-Release Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analysis is needed for an extended period of time. The controlled-release nature of the formulation allows Oxycodone It/C Controlled-Release Tablets to be effectively administreed every 12 hours (see CLINICAL PHARMACOLORY, PHARMACOLORY, PHARMACOLORY, PHARMACOLORY, administreed every 12 hours (see CLINICAL PHARMACOLORY, PHARMACOLORY, administreed every 12 hours (see CLINICAL PHARMACOLORY, pharmacolory), administreed every 12 hours (see CLINICAL PHARMACOLORY), a

Physicians should individualize treatment using a progressive plan of pain management, as outlined by the World Health Organization, the American Pain Society and the Federation of State Medical Boards Model Guidelines. Healthcare professionals should follow appropriate pain management principles of careful assessment and ongoing monitoring (see BOXED WARNING).

Initiation of Therapy
It is critical to initiate the dosing regimen for each patient individually, taking into account the patient's prior opioid and non-opioid analgesic treatment. Attention should be given to:

- (1) the general condition and medical status of the patient;
- (2) the daily dose, potency, and kind of the analgesic(s) the patient has been taking: (3) the reliability of the conversion estimate used to calculate the dose of oxycodone:
- (4) the patient's opioid exposure and opioid tolerance (if any),

(5) the Special Instructions for Oxycodone HCl Controlled-Release 80 mg, and 160 mg Tablets, or a Single Dose Greater Than 40 mg; and

(6) the balance between pain control and adverse experience

Care should be taken to use low initial doses of Daycodone HCI Controlled-Release Tablets in patients who are not already opioid-tolerant, especially those who are receiving concurrent treatment with muster leakants, sedatives, or other CNS active medications (see PRECAUTIONS: Drug-Drug Interactions).

For initiation of Oxycodone HCl Controlled-Release Tablets therapy for patients previously taking opioids, the conversion ratios from Foley, KM. (NEJM, 1985; 313:84-95), found below, are a reasonable starting point, although not verified in well-controlled, multiple-dose trials.

Seperience indicates a reasonable starting dose of Oxyrodone HCI Controlled-Release Tablets for patients who are taking non-opioid analgesics and require continuous around-the-dock therapy for an extended period of time is 10 mg q12h. If a non-opioid analgesic is being provided, it may be continued. Oxyrodone HCI Controlled-Release Tablets should be individually titrated to a dose that provides adequate analgesia and minimizes side effects.

Using standard conversion ratio estimates (see Table 4 below), multiply the mg/day of the
previous opioids by the appropriate multiplication factors to obtain the equivalent total daily
dose of oral oxycodone.

When converting from oxycodone, divide the 24-hour oxycodone dose in half to obtain the twice a day (q12h) dose of Oxycodone HCI Controlled-Release Tablets.

Round down to a dose which is appropriate for the tablet strengths available (10 mg, 20 mg, 40 mg, and 80 mg tablets).

Discontinue all other around-the-clock opioid drugs when Oxycodone HCl Controlled-Release Tablet therapy is initiated.

5. No fixed conversion ratio is likely to be satisfactory in all patients, especially patients receiving large opioid doses. The recommended doses shown in Table 4 are only a starting point, and close observation and frequent thration are indicated until patients are stable on the new therapy.

Multiplication Factors for Converting the Daily Dose of Prior Opioids to the Daily Dose of Oral Oxycodone*

	(Mg/Day Prior Opioid x	Factor = Mg/Day Oral Oxycodone)
	Oral Prior Opioid	Parenteral Prior Opioid
Oxycodone	1	
Codeine	0.15	
Hydrocodone	0.9	
Hydromorphone	4	20
Levorphanol	7.5	15
Meperidine	0.1	0.4
Methadone	1.5	3
Morphine	0.5	3

*To be used only for conversion to oral oxycodone. For patients receiving high-dose parenteral opioids, a more conservative conversion is warranted. For example, for high-dose parenteral morphine, use 1.5 instead of 3 as a multiplication factor.

in all cases, supplemental analgesia should be made available in the form of a suitable short-acting analgesic.

Oxycodone HCI Controlled-Release Tablets can be safely used concomitantly with usual doses of non-opioid analgesics and analgesic adjuvants, provided care is taken to select a proper initial dose (see **PRECAUTIONS**).

Conversion from Transdermal Fentanyl to Oxycodone HCI Controlled-Release Tablets

Controlled-Release Tablets Elighteen hours following the removal of the transdermal fentanyl patch, Oxycodone HCI Controlled-Release Tablet treatment can be initiated. Although there has been no systematic assessment of such conversion, a conservative oxycodone dose, approximately 10 mg q1 Oxycodone HCI Controlled-Release Tablets, should be initially substituted for each 25-µg/hr fentanyl transdermal patch. The patient should be followed closely for early titration, as there is very limited clinical experience with this conversion.

Managing Expected Opioid Adverse Experiences
Most patients receiving oploids, especially those who are opioid-naive, will experience side
effects. Frequently the side effects from Oxycodone HCI Controlled-Release Tablets are
transient, but may require evaluation and management. Adverse events such as constipation
should be anticipated and treated aggressively and prophylactically with a stimulant learnite
and/or stool softener. Patients do not usually become tolerant to the constipation effects of

Other opioid-related side effects such as sedation and nausea are usually self-limited and often do not persist beyond the first few days. If nausea persists and is unacceptable to the patient, treatment with antiemetics or other modalities may relieve these symptoms and should be considered.

ents receiving Oxycodone HCl Controlled-Release Tablets may pass an intact matrix "ghost" he stool or via colostomy. These ghosts contain little or no residual oxycodone and are of no clinical consequence

Individualization of Dosage

Once therapy is initiated, pain relief and other opioid effects should be frequently assessed.

Patients should be tristed to adequate effect (generally mild or no pain with the regular use of no more than two doses of supplemental analgesia per 24 hours). Patients who experience breakthrough pain may require dosage adjustment or rescue medication. Recause steady-state plasma concentrations are approximated within 24 to 36 hours, dosage adjustment may be carried out every 1 to 2 days. It is most appropriate to increase the q12h dose, not the dosing frequency. There is no clinical information on dosing intervals shorter than q12h. As a guideline, except for the increase from 10 mg to 20 mg q12h, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose at each increase.

If signs of excessive opioid-related adverse experiences are observed, the next dose may be In agio of textessive syndrometraction over experiences a construct, time new town the process of the reduced. If this adjustment leads to inadequate analysis, a supplemental dose of immediate-release oxycodone may be given. Alternatively, non-opioid analgesic adjuvants may be employed. Dose adjustments should be made to obtain an appropriate balance between pain relief and opioid-related adverse experiences.

If significant adverse events occur before the therapeutic goal of mild or no pain is achieved, the events should be treated aggressively. Once adverse events are under control, upward titration should continue to an acceptable level of pain control.

During periods of changing analgesic requirements, including initial titration, frequent contact is recommended between physician, other members of the healthcare team, the patient and the caregiver/family.

Special Instructions for Oxycodone HCI Controlled-Release 80 mg Tablets, or a single dose greater than 40 mg (for use in opioid-tolerant patients only.)

Oxycodone HCI Controlled-Release 80 mg Tablets, or a single dose greater than 40 mg, are for use only in opioid-tolerant patients only. A single daily dose greater than 40 mg, or total daily dose greater than 40 mg, are for use fall repistratory depression when administered to patients who are not tolerant to the respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

One Oxycodone HCI Controlled-Release 160 mg tablet is comparable to two 80 mg tablets when taken on an empty stomach. With a high-fat meal, however, there is a 25% greater peak plasma concentration following one 160 mg tablet. Dietary caution should be taken when patients are initially titrated to 160 mg tablets.

Supplemental Analgesia

Most patients given around-the-clock therapy with controlled-release opioids may need to have immediate-release medication available for exacerbations of pain or to prevent pain that occurs predictably during certain patient activities (incident pain).

Maintenance of Therapy
The intent of the titration period is to establish a patient-specific q12h dose that will maintain adequate analgeias with acceptable side effects for as long as pain relief is necessary. Should pain recur then the dose can be incrementally increased to re-establish pain control. The method of therapy adjustment outlined above should be employed to re-establish pain

During chronic therapy, especially for non-cancer pain syndromes, the continued need for around-the-clock opioid therapy should be reassessed periodically (e.g., every 6 to 12 months) as appropriate.

Cessation of Therapy

When the patient no longer requires therapy with Oxycodone HCl Controlled-Release Tablets, doses should be tapered gradually to prevent signs and symptoms of withdrawal in the physically dependent patient.

Conversion from Oxycodone HCI Controlled-Release Tablets to Parenteral Opioids To avoid overdose, conservative dose conversion ratios should be followed.

SAFETY AND HANDLING

Oxycodone HCI Controlled-Release Tablets are solid dosage forms that contain oxycodone, which is a controlled substance. Like morphine, oxycodone is controlled under Schedule II of the Controlled Substances Act.

Oxycodone HCI Controlled-Release Tablets have been targeted for theft and diversion by criminals. Healthcare professionals should contact their State Professional Licensing Board or State Controlled Substances Authority for Information on how to prevent and detect abuse or diversion of this product.

HOW SUPPLIED

Oxycodone HCI Controlled-Release Tablets 10 mg are round, unscored, white-colored, convex tablets imprinted with OC on one side and 10 on the other. They are supplied as follows:

NDC 52152-408-02: child-resistant closure, opaque plastic bottles of 100

Oxycodone HCl Controlled-Release Tablets 20 mg are round, unscored, pink-colored, convex tablets imprinted with OC on one side and 20 on the other. They are supplied as follows:

NDC 52152-409-02: child-resistant closure, opaque plastic bottles of 100

Oxygodone HCl Controlled-Release Tablets 40 mg are round, unscored, yellow-colored, convex tablets imprinted with OC on one side and 40 on the other. They are supplied as follows:

NDC 52152-410-02: child-resistant closure, opaque plastic bottles of 100

Oxycodone HCl Controlled-Release Tablets 80 mg are round, unscored, green-colored, convex tablets imprinted with OC on one side and 80 on the other. They are supplied as follows:

NDC 52152-411-02: child-resistant closure, opaque plastic bottles of 100

Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).

Dispense in tight, light-resistant container.

CAUTION DEA Order Form Required.



Distributed by: Actavis Totowa LLC 990 Riverview Drive Totowa, NJ 07512 USA

U.S. Patent Numbers 5,508,042 and 7,129,248 8949-00

June 2009

CII

PATIENT INFORMATION

OXYCODONE HCI **CONTROLLED-RELEASE TABLETS**

Oxycodone HCl Controlled-Release Tablets, 10 mg Oxycodone HCI Controlled-Release Tablets, 20 mg Oxycodone HCI Controlled-Release Tablets, 40 mg Oxycodone HCl Controlled-Release Tablets, 80 mg

R, Only

Read this information carefully before you take Oxycodone HCl Controlled-Release Tablets. Also read the information you get with your refills. There may be something new. This information does not take the place of Takling with your doctor about your medical condition or your treatment. Only you and your doctor can decide if Oxycodone HCl Controlled-Release Tablets are right for you. Share the important information in this leadlet with members of your

What is The Most Important Information I Should Know About Oxycodone HCI Controlled-Release Tablets?

- Use Oxycodone HCl Controlled-Release Tablets the way your doctor tells you to.
- Use Oxycodone HCI Controlled-Release Tablets only for the condition for which it was prescribed.
- Oxycodone HCl Controlled-Release Tablets are not for occasional ("as needed") use.
- Swallow the tablets whole. Do not break, crush, dissolve, or chew them before swallowing. Oxycodone HCI Controlled-Release Tablets work properly over 12 hours only when swallowed whole. If a tablet is broken, crushed, dissolved, or chewed, the entire 12 hour dose will be absorbed into your body all at once. This can be dangerous, causing an overdose, and possibly death.
- Keep Oxycodone HCl Controlled-Release Tablets out of the reach of children. Accidental
 overdose by a child is dangerous and may result in death.
- Prevent theft and misuse. Oxycodone HCI Controlled-Release Tablets contain a narcotic painkiller that can be a target for people who abuse prescription medicines. Therefore, keep your tablets in a secure place, to protect them from theft. Never gree them to anyone else. Selling or giving away this medicine is dangerous and against the law.

What are Oxycodone HCI Controlled-Release Tablets?

Oxycodone HCI Controlled-Release Tablets are tablets that come in several strengths and voycounter For Guiture-interests indicate and cate that the Chine in several strengths also contain the medicine oxycodone (ox.=-KOE-done). This medicine is a painkiller like morphine. Oxycodone HC Controlled-Release Tablest treat moderate to severe pain that is expected to last for an extended period of time. Use Oxycodone HC Controlled-Release Tablest regularly during treatment. It contains enough medicine to last for up to twelve hours.

Who Should Not Take Oxycodone HCI Controlled-Release Tablets?

- who should not rake Cxycodone HC controlled-Release Tables if

 your doctor did not prescribe Oxycodone HCI controlled Release Tablets for

 your doctor did not prescribe Oxycodone HCI controlled Release Tablets for you,

 your pain in mild or will go away in a few days.

 your pain can be controlled by occasional use of other painkillers.

 you have severe astima or severe lung problems.

 you have had a severe allergic reaction to codeine, hydrocodone, dihydrocodeine, or oxycodone claws a fylox, Tylend with Codeine or Vicodini. A severe allergic reaction to codeine, with the controlled severe rash, thirds, breathing problems, or dizziness.

 you had surgerly less than 12 24 hours ago and you were not taking Oxycodone HCI Controlled Release Tablets just before surgery.

Your doctor should know about all your medical conditions before deciding if Oxycodone HO Controlled-Release Tablets are right for you and what dose is best. Tell your doctor about all of your medical problems, especially the ones listed below:

- · trouble breathing or lung problems

- head injury liver or kidney problems adrenal gland problems, such as Addison's disease convulsions or seizures

- hallucinations or other severe mental problems
 past or present substance abuse or drug addiction

If any of these conditions apply to you, and you haven't told your doctor, then you should tell your doctor before taking Oxycodone HCI Controlled-Release Tablets.

If you are pregnant or plan to become pregnant, talk with your doctor. Oxycodone HCI Controlled-Release Tablets may not be right for you. Tell your doctor if you are breast feeding. Oxycodone HCI Controlled-Release Tablets will pass through the milk and may harm the baby.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. They may cause serious medical problems when taken with Oxycodone HCI Controlled-Release Tablets, especially if they cause drowsiness.

How Should I Take Oxycodone HCI Controlled-Release Tablets?

- Follow your doctor's directions exactly. Your doctor may change your dose based on your reactions to the medicine. Do not change your dose unless your doctor tells you to change it. Do not take Oxycodone if ICI Controlled-Allease Tablets more often than prescribed.

 Swallow the tablets whole. Do not break, crush, itsosive, or chew before swallowing. If the tablets are not whole, your body will absorb too much medicine at one time. This can lead to serious problems, including overdose and death.

 If you miss a dose, take it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not take 2 doses at once unless your doctor tell's you to.
- In case of overdose, call your local emergency number or Poison Control Center right away.

 Review your pain regularly with your doctor to determine if you still need Oxycodone HCI Controlled-Release Tablets.
- You may see tablets in your stools (bowel movements). Do not be concerned. Your body has already absorbed the medicine.

If you continue to have pain or bothersome side effects, call your doctor

Stopping Oxycodone HCl Controlled-Release Tablets. Consult your doctor for instructions on how to stop this medicine slowly to avoid uncomfortable symptoms. You should not stop taking Oxycodone HCl Controlled-Release Tablets all at once if you have been taking it for more than a few days.

After you stop taking Oxycodone HCl Controlled-Release Tablets, flush the unused tablets down the toilet.

What Should I Avoid While Taking Oxycodone HCl Controlled-Release Tablets?

- Do not drive, operate heavy machinery, or participate in any other possibly dangerous activities until you know how you react to this medicine. Oxycodone HCl Controlled-Release Tablets can make you sleepy.
- Do not drink alcohol while using Oxycodone HCI Controlled-Release Tablets. It may increase the chance of getting dangerous side effects.
- Do not take other medicines without your doctor's approval. Other medicines include prescription and non-prescription medicines, vitamins, and supplements. Be especially careful about products that make you sleepy.

What are the Possible Side Effects of Oxycodone HCI Controlled-Release Tablets?

Call your doctor or get medical help right away if

· your breathing slows down

· you feel faint, dizzy, confused, or have any other unusual symptoms

Some of the common side effects of Oxycodone HCl Controlled-Release Tablets are nausea, vomiting, dizziness, drowsiness, constipation, itching, dry mouth, sweating, weakness, and headache. Some of these side effects may decrease with continued use.

There is a risk of abuse or addiction with narcotic painkillers. If you have abused drugs in the past, you may have a higher chance of developing abuse or addiction again while using Oxycodone HCI Controlled-Release Tablets.

These are not all the possible side effects of Oxycodone HCI Controlled-Release Tablets. For a complete list, ask your doctor or pharmacist.

General Advice About Oxycodone HCI Controlled-Release Tablets

- Do not use Oxycodone HCl Controlled-Release Tablets for conditions for which it was not
- Do not give Oxycodone HCI Controlled-Release Tablets to other people, even if they have the same symptoms you have. Sharing is illegal and may cause severe medical problems, including death.

This leaflet summarizes the most important information about Oxycodone HCl Controlled-Release Tablets. If you would like more information, talk with your doctor. Also, you can ask your pharmacist or doctor for information about Oxycodone HCl Controlled-Release Tablets that is written for health professionals.



Distributed by: Actavis Totowa LLC 990 Riverview Drive Totowa, NJ 07512 USA

302173-0A 8949-00 Rev 06/2009